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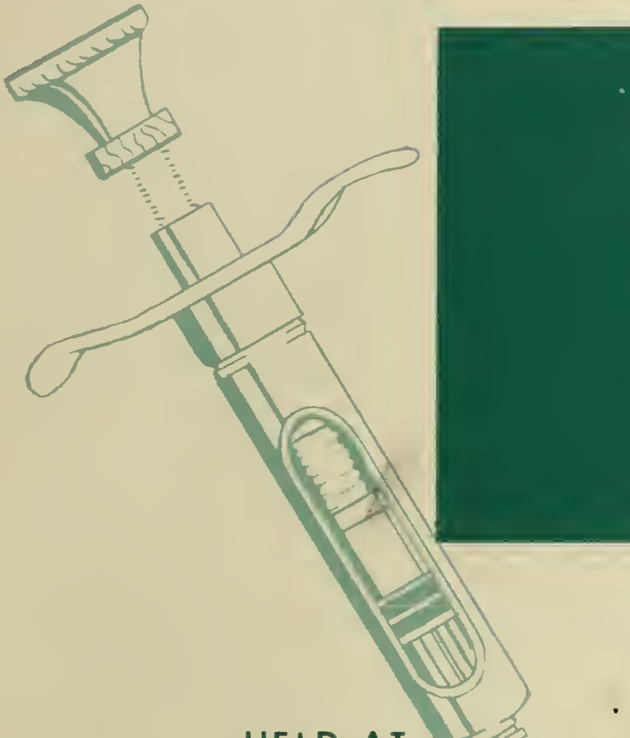

TUBERCULOSIS ERADICATION CONFERENCE

HELD AT
College of Veterinary Medicine
Michigan State University
East Lansing, Michigan
JUNE 16-20, 1958

Agricultural Research Service
UNITED STATES DEPARTMENT OF AGRICULTURE

FOREWORD

This publication contains most of the presentations given at the Tuberculosis Eradication Conference sponsored by the Agricultural Research Service, Animal Disease Eradication Division, at the College of Veterinary Medicine, Michigan State University, June 16 - 20, 1958.

The separate articles are digests of the professional viewpoints and experience of some of the nation's outstanding authorities on tuberculosis and its eradication. We recognize that many statements in this publication are not new, but compiling these papers into one report makes a comprehensive reference source for those interested. After reviewing the papers we find that the information within them summarizes the problems that exist today in the eradication of bovine tuberculosis.

The information contained herein provides for a better understanding of the propagation of tuberculosis and the important causative factors. Also included are recommendations for effective procedures in overcoming some of the major problems associated with the eradication of tuberculosis from our domestic livestock. It is clearly indicated that we cannot drift along and arrive at our goal of eradication without the active support of the entire livestock industry for which the program is maintained.

A. F. Ranney

A. F. Ranney, Chief Staff Officer
Tuberculosis Eradication
Animal Disease Eradication Division
Agricultural Research Service

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WELCOME

Dean W. W. Armistead, College of Veterinary Medicine
Michigan State University, East Lansing

As most of you realize, ordinarily the governor or mayor is listed on your program to give the welcome address. Then at the last minute some wild-eyed young fellow rushes in all out of breath to explain that "his honor" couldn't be here so he is pinch-hitting.

In this case there is no welcome address listed on your program, so anything you get is likely to be better than what had been scheduled. At least I hope it will be.

It is a pleasure to welcome you, if a welcome is necessary. Welcome addresses are very much standard operating procedure, and it is considered heresy to consider omitting them, so we have included a welcome address -- and one that can be entirely sincere.

This kind of conference is the type of thing that Michigan State University has always enjoyed participating in. As a land-grant institution, we try to live by our philosophy of being of maximum service to the people from whom the university has sprung. For that reason, it's a real pleasure to welcome you here -- even though a welcome isn't really necessary, because at Michigan State you are always welcome.

This was the first of the agricultural colleges, the pioneer land-grant college, and we feel that in a way it is fitting that this tuberculosis conference should be held at East Lansing.

This, of course, is an age of specialists, and for that reason it becomes more important as the years go by that we all get together to sit down, compare notes, and take stock of accomplishments. This is the reverse of "keeping up with the Joneses" because in animal disease control and animal disease research, not keeping up with the Joneses can be highly fatal.

It is important that we have an occasional opportunity to compare our progress with the progress that is being made by others working in the same or related areas. Some of you may remember the befuddled little scientist in Gulliver's Travels who had been laboring in his dark, dingy laboratory all by himself for 8 years trying to discover a way to extract moonbeams from cucumbers. This didn't seem at all unusual to him because he had been working by himself so long that he had no way to compare his efforts

with the efforts of others. There is a danger that this sort of thing can happen to all of us, and that is one big reason why I think this kind of conference is so important.

I hope that while you are here, although you are here primarily for business, you will take time to get acquainted with Michigan State, to see what I think certainly must be one of the loveliest campuses in the United States, and to get acquainted with the staff and facilities of the Veterinary College, of which we are naturally rather proud.

I think those of you who are Michigan State alumni will see evidence of considerable growth, particularly in the past few years. For example, the enrollment at Michigan State has increased from about 15,000 to about 20,000 students in the past 3 years. Obviously, 33 percent growth in a period of 3 years is a tremendous amount of progress.

You can see the marks of growth on the campus in the way of new buildings and crowded facilities. The Veterinary College here is a bit unique in that we teach all of the physiology, all of the anatomy, and all of the microbiology for the entire university. In addition, the College of Veterinary Medicine has under its administration a medical technology curriculum in which we have about 118 women enrolled.

Our total enrollment in the College of Veterinary Medicine is in the neighborhood of 600 students. Of course, only about 245 of those are DVM candidates. The others are medical technology students, majors in zoology and physiology, and also students taking part in our sizable graduate program.

Once again, I would like to tell you how welcome you are, how glad we are to have you at Michigan State, and how happy we are to be a part of the sponsoring agency for this fine conference. And I would like to thank you for the privilege of welcoming this group. I know you will have a successful and fruitful conference, and if there is any way in which we can be of help to you, I hope you will feel free to call on us.

It is customary for the man giving the welcome address to offer the key to the city. No key is necessary for this city; we're glad to turn everything over to you while you are here. It is also customary for us to offer to get you out of a jam with the local constabulary if you should have any such difficulty. Unfortunately, or perhaps fortunately in this case, disciplinary and police matters are out of the realm of an academic dean, so we can't be a great deal of help. However, I suspect you will not need such help. Without belaboring you any further, I would again like to say "Welcome!"

OPENING CONFERENCE STATEMENT

Asa Winter, Animal Disease Eradication Division
ARS, USDA, Lansing, Mich.

As a local resident and representative of the Animal Disease Eradication Division, I am pleased that the program committee has given me the opportunity to open this conference, which I sincerely believe to be of real significance to the livestock industry and general public of this nation.

It has been a long time since we have held a tuberculosis conference anywhere nearly as stimulating as this one. We never have held a conference of this scope. I recall attending several regional conferences during the early period of our tuberculosis eradication efforts but those conferences were discontinued many years ago, even before national accreditation status was attained. And following accreditation it became difficult to hold even a round table conference on tuberculosis because of the false interpretation given the national accreditation status of this country.

Too many of us, not only the veterinarians, but the livestock owners and the public in general, considered that when the country was accredited, we had eliminated tuberculosis, or had at least reached the point where it was no more a problem. Because of this attitude toward a disease situation which is again building up to a point of major importance, we feel that a conference of this nature is far overdue. Naturally, we are very happy that the State of Michigan was selected as the site for such a meeting and to have the opportunity to welcome you as participants in the program.

I'm sure, in reviewing the conference agenda, you will agree that we are very fortunate in having a list of participants and guest speakers who are leaders in the tuberculosis eradication field. It is my understanding that there was full acceptance on the part of speakers who were invited to attend this conference, except in those cases where there had been previous commitments. It is also my understanding that some of these national leaders are arriving late in the evening and must leave soon following their talks the next day in order to meet other commitments.

This effort is very much appreciated for it indicates a realization on the part of people who have been associated with this program in research and control work that we do need their support in reviewing the tuberculosis situation today.

We need to reevaluate our policies, our practices, and our procedures, and we're going to be most happy to listen to these people. And I am sure, from my own experience in attending previous conferences of a somewhat similar nature, that each attendant will return to his respective

State or position, whatever it may be, stimulated and inspired to the current significance of tuberculosis.

The success of our eradication program in the future, as in the past, must depend upon the cooperation and support of all interested agencies. The early cooperation responsible for the success of the program has died down to some extent during recent years, although support seems to be building up again in many areas.

I have been very fortunate in all of my assignments but I have never enjoyed my work anywhere more than I have here in the State of Michigan, cooperating with the State Department of Agriculture and the Veterinary College. We've had tremendous support for this program. There has been a real appreciation of the significance of tuberculosis, and I am sure that when you study the reports and our Michigan testing records, you can see why we are quite concerned and why we are truly interested in tuberculosis and the future of this project.

We could not have held this conference had it not been for a common understanding and the tremendous support given us by the Veterinary College under the leadership of Dean Armistead, and with the assistance of his staff.

We are very happy that Dr. Armistead's duties as President of the American Veterinary Medical Association and Dean of the Veterinary College permit him to be with us this morning. We hope he can spend more time with us during the week.

OBJECTIVES OF THE CONFERENCE

A. F. Ranney, Animal Disease Eradication Division,
ARS, USDA, Washington, D. C.

As you all know, the tuberculosis eradication project was started in May 1917, with the organization of the Tuberculosis Eradication Division of the former Bureau of Animal Industry.

From that time on great progress was made with tuberculosis eradication, reducing the incidence of infection from about 5 percent to below 0.5 percent when the country was accredited in 1940. Since 1940, we have had what we call a tuberculosis eradication program, but I'm sure most of us will admit that it has not been much more than a control program.

We hope this conference will be the start of a real "bang up" job leading to eradication. We have on the program people with various interests so far as tuberculosis eradication is concerned--some have given a considerable amount of time to research, others to education,

while some have worked on tuberculosis in the field and in other capacities.

We all know something of the problems with which we are faced. If we are going to eradicate the disease, and this is our goal, we must put our thoughts together, make use of the best scientific data, and really do a job.

Back in 1919, Dr. Mohler, who was then Chief of the former Bureau of Animal Industry, made this statement:

"This program has not developed because you and I have been associated with it, or by any Act of Congress or State Legislatures, but because it is worthy work and has merit in its foundation. This is the only kind of work that will succeed in the long run and is the only kind with which we should be associated."

I'm sure we all agree that we are associated together in a project worthy of the effort we are putting into it--and much more. Those of you who have been associated with the program know that it was one of the most gigantic disease eradication programs ever to be inaugurated. The accomplishments up to the time we gained countrywide accredited status were no less than stupendous. But we must realize that the enthusiasm that goes into a program such as this is easy to obtain at the outset, but it is not easy to maintain during the long hard pull to the ultimate goal.

We have now reached the point where we must pick up the loose ends and push the program through to complete eradication. We have reached a stage where the incidence of disease is low enough to be difficult to find, yet is prevalent enough to be exceedingly dangerous. For that reason we are always faced with the possibility that it will get a foothold and cause a much higher incidence of infection than we have at the present time.

Now there are four points that I particularly want to bring out: One is that we must give greater attention to the application of tuberculin tests. Due to the low incidence of infection and the infrequency with which some of us find reactors, we may feel that we aren't going to find reactors. From that point we become careless and complacent and probably fail to give the test the attention it should have. Another point I would like to emphasize is that we must give more attention to the diagnostic interpretation of the test and use good judgment in handling all herds in which the disease is found. In addition we must intensify our epidemiological studies, or tracing procedures--tracing of diseased animals found on regular kill, the tracing of the origin of reacting animals, and the follow-up of exposed animals. These must be made an integral part of our program and are natural adjuncts to the testing phase. My final point is that we must develop and maintain

procedures designed to prevent reinfection and spread of the disease. We must not casually test a herd, remove the reactors, and fail to seek the cause of the infection or to take all steps necessary to prevent its continuation on the premises. It's just as important to study the sanitary conditions of infected premises as it is to test the herd.

The problem of tuberculosis eradication presents a real challenge and I'm sure if we work together in a cooperative manner, taking all of the essential facts into consideration, we will be successful. Our thinking on these problems must be all-inclusive. Proper attention must be given not only to the big things but to the small points which, if neglected, are likely to lead us to disaster.

We anticipate that as a result of this conference we will have a representative in each State who will be not only better trained and in a better position to point out the problems that face us, but one who can help us to develop more uniformity in the tuberculosis eradication program including the application of standard testing procedures. We must keep in mind that the livestock owners of this country expect service from us, and we must conduct this program in such a manner as to merit their respect and confidence.

Tuberculosis eradication will not result from the enterprise of any one State or of the Federal Government. This is a cooperative endeavor in which each unit must do its share. We must rededicate ourselves to pursuing this program with enthusiasm and vigor. It must be carried through, without delays of any kind, until the disease has been eradicated.

A DIRECTOR OF AGRICULTURE'S LOOK AT TUBERCULOSIS ERADICATION

G. S. McIntyre, State Department of Agriculture
Lansing, Mich.

I want to welcome all of you to Michigan and to commend those Federal officials who are responsible for setting up this meeting. We feel that this meeting is not only desirable, but that it is necessary. We are glad that this meeting is being held, first, to place emphasis upon the tuberculosis eradication program; secondly, because there still seems to be a lot to be learned about bovine tuberculosis; thirdly, because we feel there is a need for uniform techniques in applying and reading the tests; and fourth, because there is need for reappraisal and an overhauling of the entire TB eradication program.

We, in Michigan, are concerned, and we are not sure that we should be alone in our concern. Our experience, along with that of some of our neighboring States, leads us to believe that there should be a complete

reappraisal of the entire TB eradication and county accreditation program, and that this reappraisal should be undertaken immediately.

Michigan is in a critical situation as far as bovine TB is concerned. During the past 2 or 3 years, Michigan has been slaughtering 20 percent or more of all the TB reactors slaughtered in the United States. While we feel this may give a false impression of the incidence of TB in Michigan, we believe it does point up the need for this meeting. Only by frank discussion and appraisal can a program be developed that will eradicate TB.

The TB eradication program in Michigan was started in 1922. At that time the incidence of the disease was better than 4 percent. During the years following 1922, the incidence of the disease declined until just prior to World War II, when it reached a low point of 0.17 percent. Since that time it has increased every year until, in 1957, the average incidence in the State as a whole was 0.8 of one percent. Some areas of the State have a much higher incidence. Why has this increase occurred? We think there are several reasons.

1. There was an increase in a highly mobile cattle population. In 1922 Michigan had 1.5 million head of cattle. In 1955 that total had increased to 2 million head. In 1957 it had dropped back to 1.9 million head. During the years following World War II transportation was much better, roads were much better, and cattle moved freely. In addition, since 1937 there have been 60 livestock auction sales established in Michigan. These sales are selling approximately 350,000 head of cattle each year.

2. There has been a decrease in the number of cattle tested. During the 5 year period 1922 to 1926 we tested on an average 400,000 head yearly. During the years 1940 to 1942 the number dropped to 250,000. In 1957 it had climbed back up to 500,000 head. Yet during the period 1937 to 1955, expenditures for TB eradication in Michigan changed very little.

3. We think there has been apathy and a lag in interest in TB testing. Farmers thought the battle was over. They had little concern about it. Veterinarians were lax in their testing and in the reading of tests, and there was also the problem of new inexperienced veterinarians. There was a lack of uniformity in applying and reading the test. In many cases we have found that herds were skipped on official tests of a township.

4. State and Federal officials were giving more of their attention to brucellosis and did not consider the tuberculosis problem to be a major one. Both groups of officials let appropriations for the TB testing programs dwindle.

There were a number of other reasons for this increase, too. Such things as an increase in the number of susceptible animals, the fact that many herds were missed on official tests, and a lack of central control of the testing program were all contributing factors.

Now what was the result of all of this? In Michigan we found ourselves in a serious situation. In 1955 we found ourselves behind in testing for reaccreditation, and I might say those untested counties were still officially accredited. In a county with the largest number of cattle, the incidence jumped to nearly 2 percent, and in another county the incidence in one township was 5 percent. The incidence of the disease was high in other parts of the State, and the overall average jumped to 0.8 percent.

It is somewhat doubtful that 0.17 percent was correct under the testing procedures that were used in 1940 but, regardless of that, the incidence under the new testing procedures did increase.

How did we overcome this situation? In 1954 we took steps to correct the deficiencies in the Michigan TB eradication program. We reappraised the entire program to see what should be done and we took the following steps:

1. We had a complete reorganization of the administration of the program. Prior to 1955, the program was jointly administered by the State Veterinarian and the Federal supervisor. Neither had complete authority over the program. This resulted in some confusion and a division of personnel into Federal employees and State employees.

   We believe a disease control program within a State is a State responsibility, and the State should take the initiative in its control. We believe, secondly, that the Federal Government has a responsibility to protect other States, and to that extent should assist the States in their programs and, third, we believe there must be close cooperation between State and Federal Governments in any program if funds are to be wisely expended and the greatest amount of good is to be realized from those expenditures.

   Whenever there is a lack of complete cooperation and coordination between Federal and State officials, it is the livestock producers who suffer, not the Federal or State agency.

   We therefore proceeded to set up an organization in which each individual would know his exact responsibility and to whom he was responsible. We now have area veterinarians in charge of work in two, three, four, or more counties who are supervised by a district veterinarian. We have six such district veterinarians in the State. In turn the entire State tuberculosis program is under the direction

of Dr. R. M. Scott, who is responsible to Dr. Asa Winter and his Assistant, Dr. C. L. Hendee.

In this organization we are not primarily concerned whether a veterinarian receives his pay from the Federal Government or the State, except that we do have three district veterinarians who are State employees and three district veterinarians who are Federal employees. This is done to help maintain proper morale in each agency. Beyond that we are not concerned about who an individual is working for. There are Federal veterinarians working under the supervision of State men and State veterinarians working under the supervision of Federal veterinarians.

We have no room or time for jealousies between agencies either in the State office or among field personnel. I do not have the fear, as some folks do, that the Federal Government is going to take over Michigan's TB or brucellosis programs.

In the first place, the Federal Government would not be here if we did not want them, and in the second place, in less than 1 minute the Director of Agriculture can remove their authority to enter upon private property. It would be very difficult for them to carry on much of a testing program without being vested with State authority.

We do not anticipate any trouble along this line, because in Michigan neither the State nor the Federal Government is interested in receiving credit for work done. We are only interested in getting the job done. If we don't get it done, the livestock owners and the public lose and I maintain that if credit is due, it will be received and need not be asked for.

2. We alerted farm organizations and health groups to the increase in TB and gained their support.

3. We conducted an educational program with the help of the Extension Service and county agents, Michigan Veterinary Medical Association, and a farm publication, the Michigan Farmer.

4. We requested additional funds to carry on the testing program from the State legislature and the Federal Government, and both responded readily.

5. We installed an IBM system of record keeping. This resulted in two important changes in the program. First, it provided complete central control at the State level. Before the IBM installation control was scattered throughout the State. There is now a complete file on every herd in Michigan in the State office. In addition, we now know when a herd is tested or not tested. Before the IBM

system was installed we did not know and we found some highly infected herds that had not been tested for 12 years or more.

6. We established a very strict and rigid quarantine policy on herds that were found to be infected with tuberculosis.

Michigan is now proceeding with a testing program which we feel confident will eradicate TB from Michigan herds. I feel that the TB testing and accreditation programs need a reappraisal. I am sure this thought is shared by other Commissioners, Secretaries, and Directors of Agriculture.

I believe that accreditation should mean something. It should be based on a testing program that will include all cattle at periodic intervals, with the possible exception of range cattle. I believe accreditation should be withdrawn when a county has not been tested at predetermined intervals. A realistic accreditation program will encourage testing.

Many States, including Michigan, permit importation of cattle without test from accredited counties. If accreditation does not mean more than it has in the past, then State laws must be changed for protection of the State. Unless that protection is given, Michigan is going to have to change its law to require the testing of all cattle for TB before they enter the State regardless of where they come from.

I feel, too, that accreditation should not under any circumstances be considered as the final goal in TB eradication. It should only be a milepost toward complete eradication of the disease. It should not lead any State to decrease the amount of testing for tuberculosis.

There must also be developed and put into use standardized testing techniques to be used by State, Federal, and local veterinarians when conducting TB tests. I am led to believe there are variations in the application of the test and readings by different veterinarians.

I feel that the State and Federal Governments are going to have to expend more funds for TB eradication, and livestock owners must feel a responsibility to test their herds periodically at their own expense.

In Michigan, we have learned that if you do not test cattle tuberculosis can again show its ugly head. And we are learning it from very bitter experience that it is necessary to test and continue to test and do it on a realistic program. If we can hold down the incidence of the disease, the cost of testing is not so

great, but when we test and find a high incidence of the disease and pay indemnity on the condemned animals, the cost increases materially. It is for these reasons that I feel the tuberculosis eradication program must be reappraised and overhauled if we expect to eradicate this disease from the United States.

I hope this conference will result in such a reappraisal and the adoption of standard techniques. I feel that this is a real challenge. Because of the health, as well as the economic aspects of TB, we must not fail.

THE CONTINUING CHALLENGE OF BOVINE TUBERCULOSIS

Asa Winter, Animal Disease Eradication Division
ARS, USDA, Lansing, Mich.

After listening to these various papers, I am sure we will agree that bovine tuberculosis is a continuing challenge. We still have too great an incidence of the disease in Michigan and in other areas, and I am a bit embarrassed because of the continuing problem since I have been personally associated with this work over a long period of time. True, it is a continuing challenge, but a challenge can always be met, and we feel confident that this conference is going to provide background that will assist greatly in meeting that challenge.

After we have worked for more than 40 years to eradicate a disease of such national significance, with an expenditure of more than 325 million dollars and with continuing annual cooperative appropriations of between 5 and 6 million dollars, we should realize that we must carefully review all policies and procedures if we are to justify such expenditures of public funds.

In speaking to veterinary groups as a whole, we find that many of the younger members have never been associated to any extent with bovine tuberculosis. With the common attitude that is displayed by so many people regarding the disease and their lack of contact with the problem, it is only natural that our younger veterinarians, in many instances, do not fully appreciate the continuing significance of tuberculosis.

This situation is being gradually overcome through demonstrations at the veterinary colleges to further orient the graduating classes regarding the disease, the latest information on the testing techniques, and how to meet the challenge as they enter various areas of practice.

In order to effectively discuss a subject like this, we should provide some background as to what has been done, what our thinking is

for the future, and why we should consider the possible need for some modification of the present plans and practices if we are to carry through to our goal of eventual eradication.

The following charts are used here as aids to further discussion of our subject. Some of them have been used at other meetings. You may be familiar with those that cover past history since those naturally remain fixed in nature, while others are being constantly revised to picture what we hope will be a constantly improving program status.

Figure 1 indicates the spread and extent of infection in this country at the time an appraisal of the situation was first made in 1917. The black area covers that particular part of the country in which most of our early infection was revealed. It is only natural that this would be identified as the high incidence area when we realize that our early breeding stock came from several of the European countries, where tuberculosis was quite common, with New York the primary port of entry.

And, as agriculture and the livestock industry spread into the New England States and west through the fertile areas of the North Central States, the disease likewise spread, something like a tidal wave. This area in the North Central and Northeastern States plus the State of California has accounted for more than 90 percent of the tuberculosis reactors that have been located in this country. It is of interest to note that we are holding our conference today right in the center of this region.

Figure 2 identifies those States in which 75 percent of the total reactors for the country have been uncovered and removed. You will notice that 10 States are identified in this group with Michigan and Indiana not yet included. Three million of the four million reactors located to date were revealed in these blocked out States.

Figure 3 illustrates the interesting fact that 50 percent of our total reactors, or roughly two million animals, were removed from the four States, New York, Pennsylvania, Iowa, and California. California, as a heavy importing State during the period prior to accreditation of the country, suffered equally with the heavily dairy populated States in the Northeastern and North Central areas.

In Figure 4, New York State presents a picture which is only logical when we consider that the early importations arrived in this area and that New York State was the heavy dairy area responsible for supplying New York City with these products. Twenty-five percent (25%) of all the reactors located in this country, or approximately one million animals, have been removed from the herds of New York State as tuberculosis infected. This is approximately one-half the normal cattle population of the State.

We are not proud of the fact that New York State has had to suffer in this manner but we credit the cooperative agencies of the State with having done a tremendous job in eliminating infection from its herds. The records show that one of the intensive dairy counties of New York State suffered loss of reactors during the accreditation period in excess of its total cattle population. Because of the difficulty of obtaining adequate replacements, the retesting procedures were responsible for removing so many animals that the final number of reactors was greater than the cattle population.

The bar graph in Figure 5, indicates the trend in national infection rate from initiation of the program in 1917 until 1957. You will note that the first bar of this graph indicates an anticipated 5-percent infection rate when the program was started. This was proven to be quite factual as an average for the country. With a cattle population of approximately 65 million animals in 1917, a 5-percent average infection rate would have resulted in 3,229,000 reactors. At the time the country was accredited in 1940, as a result of initial tests and retests, about 3.7 million reactors had been removed. The records showed an average infection rate of 0.46 percent of the cattle under test.

Many States had been accredited prior to 1940 and the testing conducted during that year included only 18 percent of the total cattle population, which was then approaching 70 million animals. The testing conducted on this 18 percent of our cattle population revealed 64,000 reactors. It was calculated on this basis that 314,000 reactors would have been located if the entire cattle population of the country had been under test. This means that about 250,000 potential reactors were not identified.

At that time we were averaging about 2.5 reactors per herd, which would mean that there were still approximately 100,000 potentially infected herds throughout the country. Naturally animals from these herds, including the possible reactors, were privileged to move without restriction and without the knowledge that infected and exposed animals were continuing to jeopardize the industry and the program of eradication. We must recall too that with accreditation of the country, too many of us, both as members of the livestock industry and our own profession, were inclined to believe that tuberculosis could, for the most part, be ruled out as a further menace.

During the period of 1952 to 1954, we reached our low point in the incidence of tuberculosis. The reported infection rate, which was calculated on the basis of retesting about 10 percent of our cattle population, averaged 0.11 percent during those 3 years. Again it was calculated that if we had tested 100 percent of the cattle population, approximately 100,000 reactors would have been revealed. Since about 10,000 were actually identified, this would leave 90,000 potential reactors, involving herds with a population of approximately 1,800,000 animals either infected or exposed as unidentified and free to move.

In 1957 there was a definite rise in the average infection rate of cattle under test. As in the past, the actual testing involved only about 10 percent of the total cattle population. This rise in infection rate has been gradual but consistent since 1954. This gradual increase in infection rate has been stressed by other speakers as one of the significant considerations that must be given careful study by our research workers and disease control officials.

On the same basis as our former calculations, if we had retested all cattle in 1957 instead of the 10 percent which revealed approximately 14,000 reactors, we would have located a total of 140,000 reactor animals, which means that approximately 125,000 probable reactors were not identified. These animals, plus their associates in some 65,000 herds, constitute a continuing barrier to the program.

It is my understanding that when the 1958 figures are computed, it is quite probable an even higher infection rate than that recorded in 1957 may be revealed. The trend indicated by these data give us considerable food for thought. I am confident that there will be discussions later on during the conference that will stress these points.

Figure 6 gives us a visual picture of the trend of the infection rate from the initiation of the program in 1917 to the present. There was a fairly consistent and quite rapid rate in reduction of the disease down to 1940, when the country was accredited with a reported 0.46 percent rate of infection. This carried along at a fairly consistent level with some slight undulations during the years 1940 to 1954, when the gradual rise mentioned in Figure 5 became quite obvious.

Figure 7 gives us a little better picture of the period from 1940, at the time of national accreditation. Reduction was quite rapid and consistent until 1943. During the following 3 years, with the World War II emergency our primary problem, the tuberculosis program naturally suffered. With a considerable shortage in veterinary personnel and the prime interest on the part of industry for maximum production without due thought to disease control, there was a very noticeable rise in the tuberculosis infection rate.

While the maximum rate of infection reached during this period was not serious as a general average, still from the percentage standpoint, it was a definite indication of what could happen if our interests should wane over any considerable period. Actually during this short period the incidence of infection rose more than 33 percent over the minimum reported in 1943. This is a clear-cut demonstration of how rapidly tuberculosis can increase when we do not follow careful herd-management practices and control procedures.

From 1945 to 1957, Figure 7, is self-explanatory since it correlates with our previous discussion of the infection trend during the years 1952,

1953, 1954, and the present continuing rise. Where we go from here depends to a large extent on what may be decided at this conference and future studies which may be made as a means of further evaluating our position.

Figure 8 has been introduced somewhat reluctantly. The solid line portion is actually a duplicate of the previous chart but a record of the State of Michigan has also been included by dotted lines to give a comparative picture of the national status as related to the current situation in Michigan. The position of this State was well described earlier. We are naturally very concerned over the situation in which we find ourselves. We are not too sure that this has developed only during the period in which we have been identifying so many reactors, since our procedures have been revised during the past two years to provide for a much more thorough coverage of areas assigned out for retest than had been previously possible.

This has given us greater assurance that all herds are now under test and it is quite evident that some of our infection has been revealed directly from those herds that had not been properly accounted for on previous retests or because of movements from such herds.

In order to provide a more complete inventory of the herd and cattle population, a farm-to-farm milk pickup was accomplished 2 years ago and all herds were properly recorded, both for brucellosis testing and reaccreditation purposes. Since July 1, 1957, the policy of this State has been to test all herds within a county for reaccreditation purposes.

When an area is designated for retest by a certain veterinarian, an assignment chart including the names of all known herd owners is provided for his information, with a copy to the area veterinarian. The testing veterinarian is directed to complete a test on all listed herds and any others that may come to his attention.

If herds listed for testing have since been disposed of, a complete record is to be obtained regarding the dispostion of animals. Until the assignment is completed, and approved by the area veterinarian, the testing veterinarian's reports are not given final acceptance. We have found that testing under this full coverage procedure has been one of the key factors responsible for the reported increase in number of reactors.

We have noted in the past that an increase in volume of testing in any area has resulted in a corresponding or even greater increase in the reported percentage of infection. In 1956 four States, Illinois, Iowa, California, and Michigan, increased their testing by 42 percent. As a result, the reactors in those four States were increased by 44 percent. It would appear from such a record that if we are to eliminate the remaining tuberculosis infection, it will be necessary to provide for a much greater intensity in our testing program.

You will note how the reported infection in Michigan increased rapidly from 1953 to 1958. We now have all cattle under test in counties assigned for reaccreditation purposes. We hope at the end of a 3-year period to provide again for complete retests of many of our more heavily infected areas to determine whether the factors responsible for the recent high incidence of infection may have been eliminated.

Figure 9 is rather interesting from another angle. It indicates the relative number of condemned carcasses when the program was started as compared to 1957. From 1908, when the first meat inspection records were available, until 1917, when the tuberculosis program was initiated, there was a 100-percent increase in retained and condemned carcasses, which was a very clear demonstration of the tremendous rise of bovine tuberculosis infection taking place during that period.

In 1917, approximately 50,000 carcasses were condemned because of tuberculosis infection. At that time only about one-half the number of cattle that are under inspection today were being Federally inspected. Even though there had been no further increase in infection we would today, without the benefit of the tuberculosis program, be condemning annually 100,000 carcasses. However, as a result of the program, in 1957 less than 300 carcasses were condemned because of tuberculosis through inspection of nonreactor animals.

Even though we are vitally concerned with this disease, it must be admitted that tremendous strides have been made up to this point in the elimination of the infection. We cannot afford to approve practices or attitudes unfavorable to continued progress.

Figure 10, which provides information regarding swine showing lesions of tuberculosis on regular kill, is interesting to us from another standpoint because, as we know, swine are highly susceptible to avian tuberculosis.

In 1924, approximately 54 million swine were slaughtered and of that number some 8 million carcasses were retained due to lesions of tuberculosis. Of the 8 million retentions, 225,000 whole carcasses were condemned.

At that time, with bovine tuberculosis very common and because of the direct association of swine with cattle in many instances, it was reasonable to expect that a high percentage of our swine retention was due to infection with bovine tuberculosis. Also, because of the nature of the types of infection, it is logical to expect that a large percentage of the condemnations resulted from infection with the bovine type of the disease.

From 1924 until 1954, there was a consistent decline in the number of lesion cases but, from that point on, further decline has been very

gradual. With bovine infection reaching its low point in 1954 but with avian tuberculosis still with us, and a sensitizing factor with swine, it would now appear the continued infection rate in swine can be attributed largely to avian infection.

This is further supported by the fact that while there are still about 25 percent as many retentions for tuberculosis there are only about 4 percent as many carcass condemnations. These data would seem to indicate that one of our continuing problems in connection with the testing program is the sensitization of cattle through exposure to avian tuberculosis.

Figure 11 identifies those States in which 75 percent of the total reactors were revealed during the years 1955 to 1957. When compared to figure 10, which referred to areas previously designated as the source of 75 percent of the reactors, it is noted that the States of Indiana and Michigan are now included and Iowa, Minnesota, Vermont and Massachusetts are removed. In general, however, this is the same area of the North Central and Northeastern States that have been of major concern since initiation of the program.

At this time these States are of special significance to not only those of us who are located in the over-all area but also to members of the industry and regulatory officials located in many of the southern States. Because of a reversal in their type of agriculture, the Southern States are now looking to this area for breeding stock from which to build their industry.

During the past 3 years, statistics indicate that the percentage of reactors located in the Southern States has doubled. Until 1955 only 7 percent of the total reactors revealed in this country had been reported from the Southern States, while during the 3 years 1955 through 1957, 14 percent of the total reactors being revealed were located in these same States.

We owe a tremendous responsibility to the livestock industry of the importing States as well as to our own to do the best possible job in eliminating the sources of infection and controlling the movement of infected or exposed animals into those areas. In order to further reduce the infection and prevent the spread of infection to our cleaner areas, we should do everything possible to improve our testing procedures and impress the livestock industry with the continuing importance of good herd management procedures and disease control practices.

In addition to any improvements that may be possible in our testing procedures, herd management practices, controlled movement of livestock as a means of further reducing infection, and the trace-back to herds of origin of lesion cases on routine meat inspection are other very important factors in this effort.

Figure 12 shows that we are testing about 643 animals on our regular program procedure to locate one reactor. Through tracing of lesion cases located at Federal, State, and municipally inspected slaughtering establishments, we are testing only 39 animals for each reactor revealed. This testing of herds identified through trace-back of these lesion cases is proving a very effective procedure and one that should be expanded and improved in every possible way.

Better identification of animals going to slaughter is one of the factors that would add greatly to this particular effort. As the value of this practice is becoming established we are constantly gaining better support from all slaughtering establishments and we surely owe recognition to the inspectors who are cooperating so closely with the disease eradication veterinarians in furthering this feature of the program.

I believe we will agree that tuberculosis in cattle is a continuing challenge and that we should give careful study to every aspect of the problem if we are to make satisfactory progress in locating and removing the remaining foci of infection which are serving to continually jeopardize our efforts for final eradication.

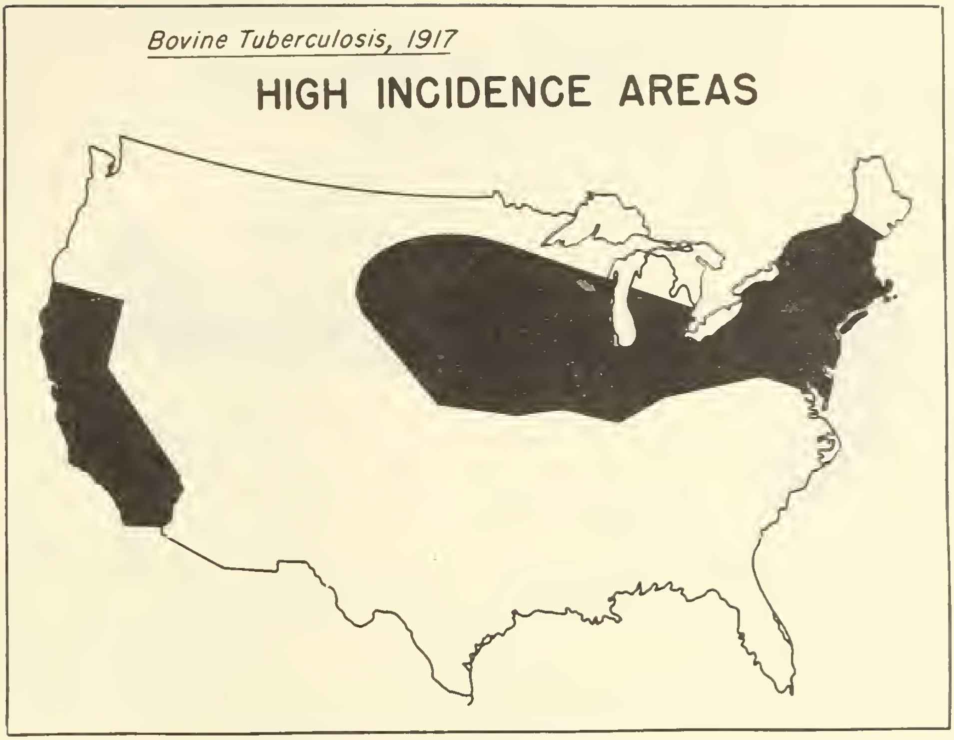


FIGURE 1 BN-9032

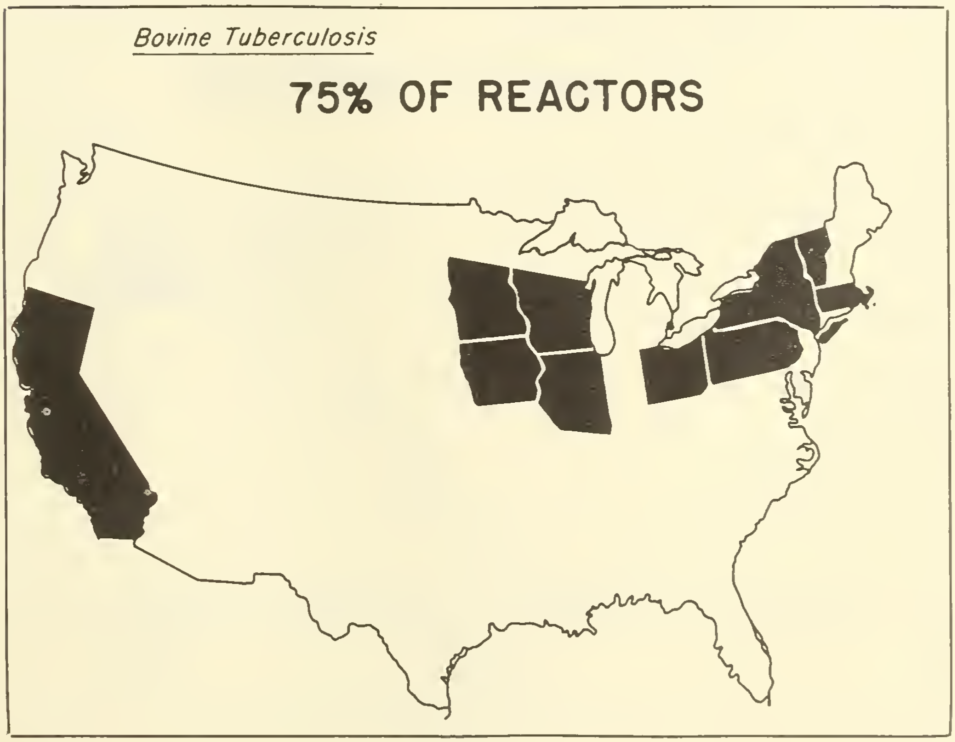


FIGURE 2 BN-9033

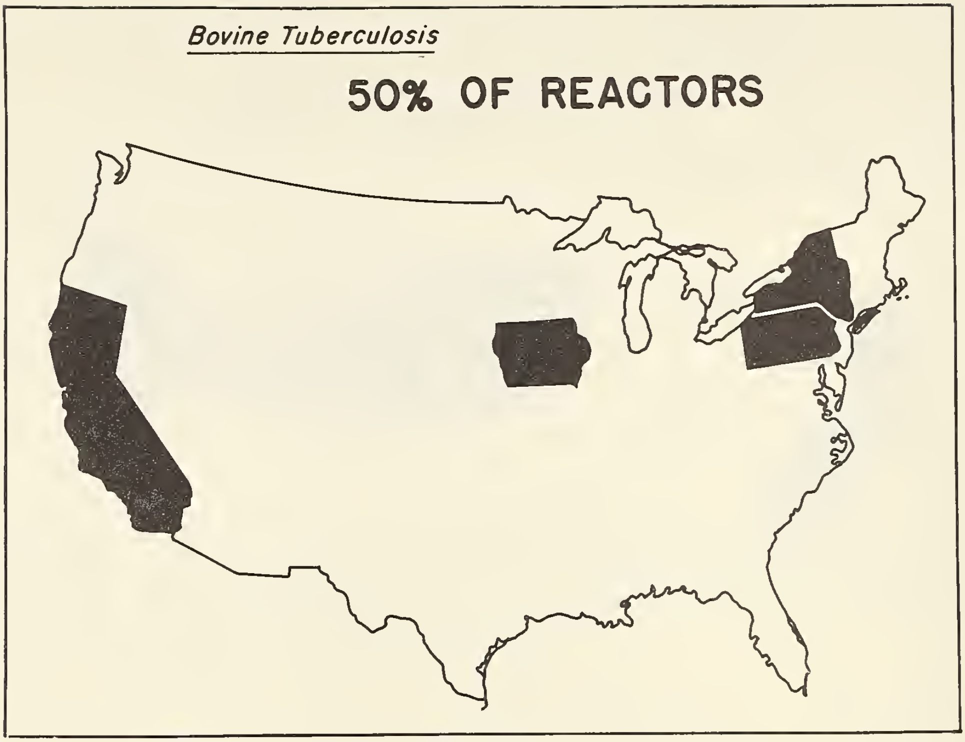


FIGURE 3 BN-9034

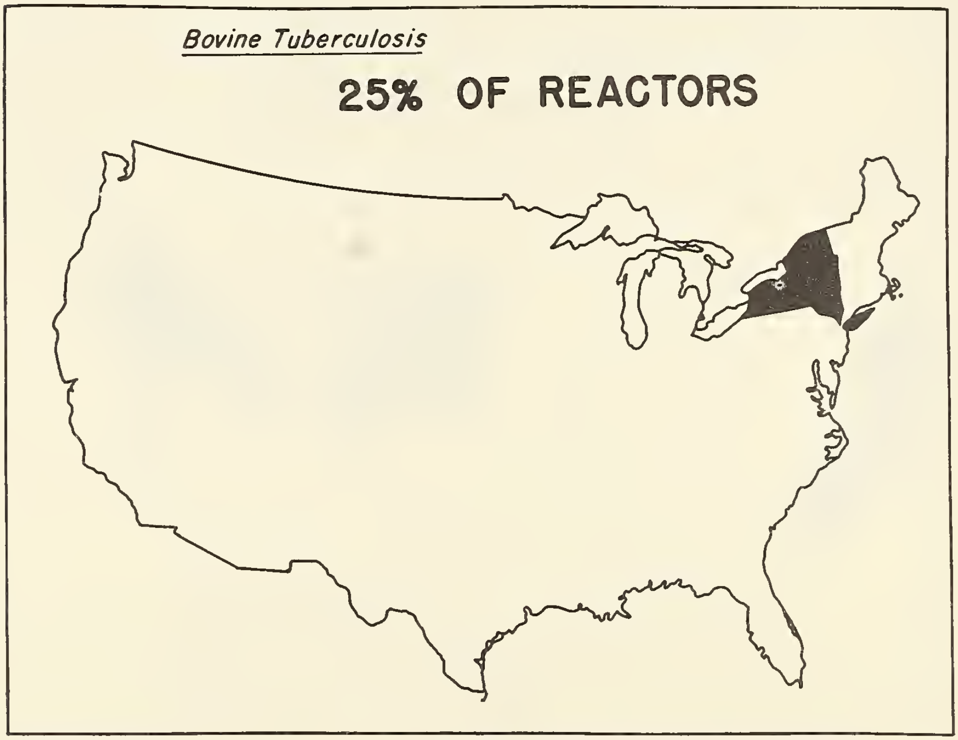


FIGURE 4 BN-9035

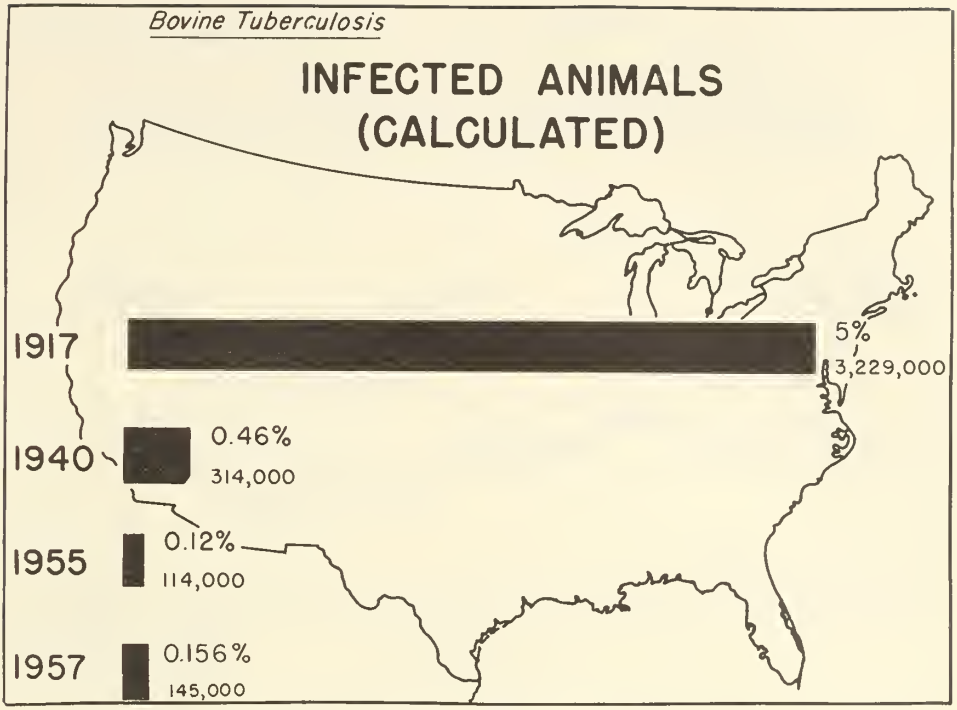
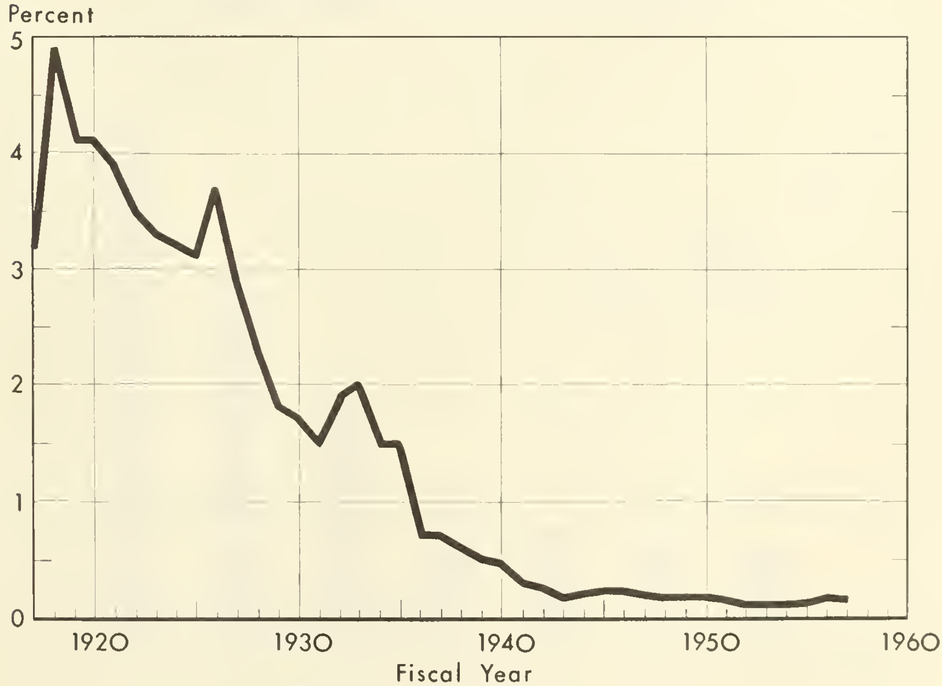


FIGURE 5 BN-9036

TUBERCULOSIS REACTORS



PERCENT BASED ON NUMBER OF CATTLE TESTED

FIGURE 6 BN-9037

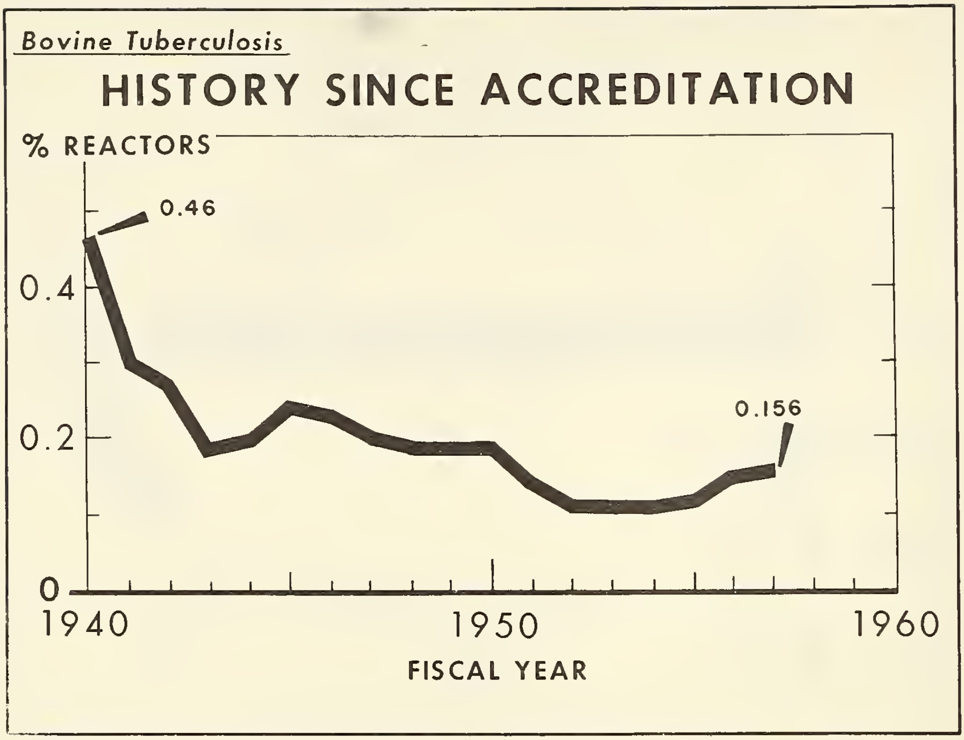


FIGURE 7 BN-9038

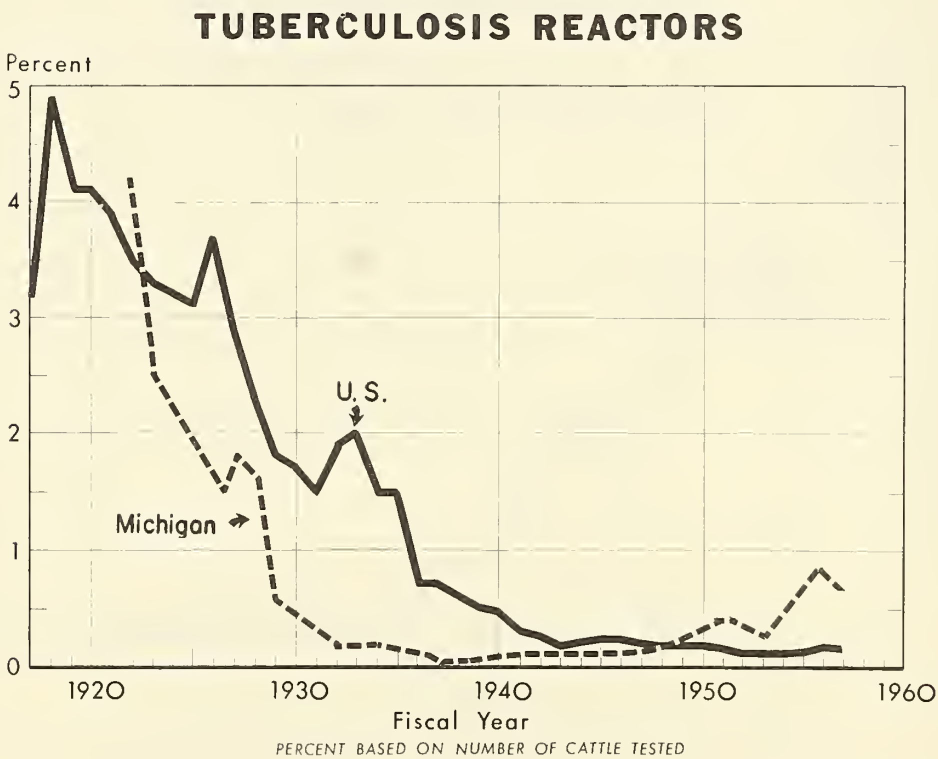


FIGURE 8 BN-9039

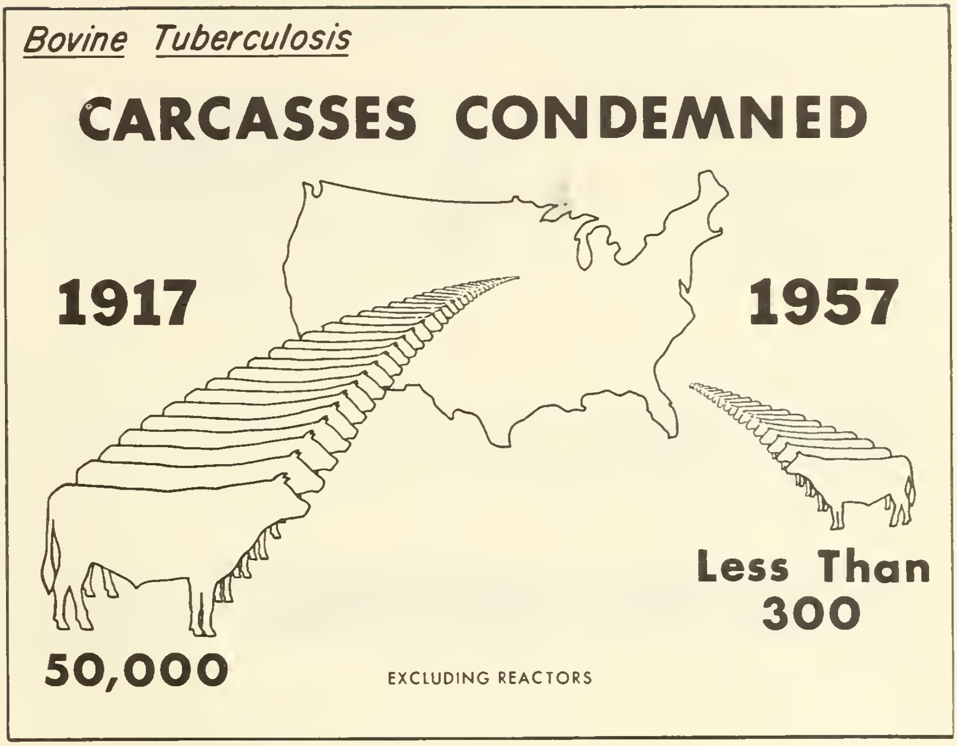


FIGURE 9 BN-9040

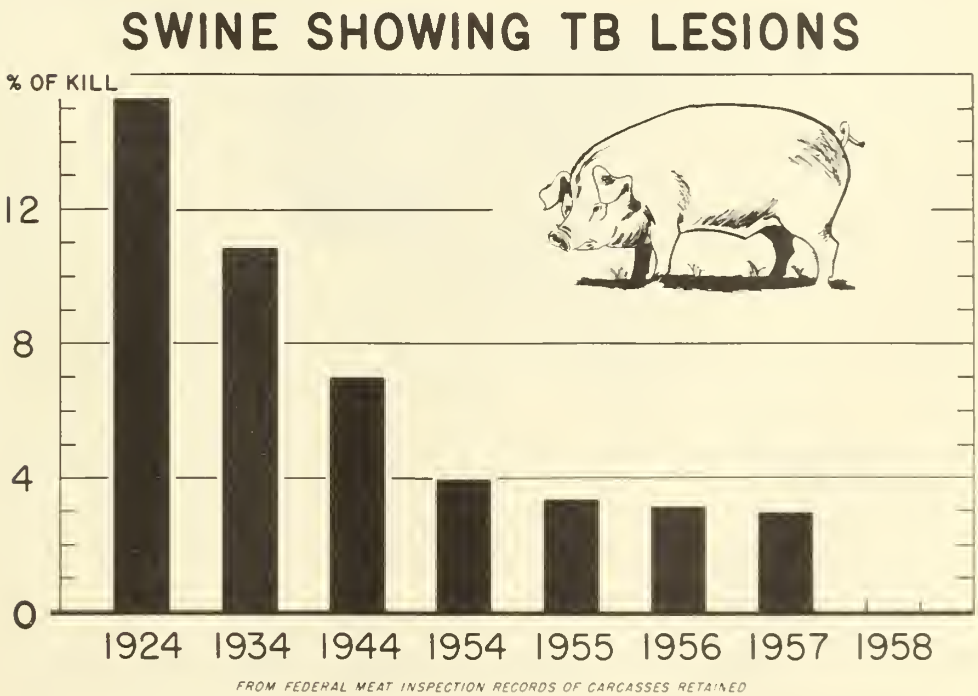


FIGURE 10 BN-9041

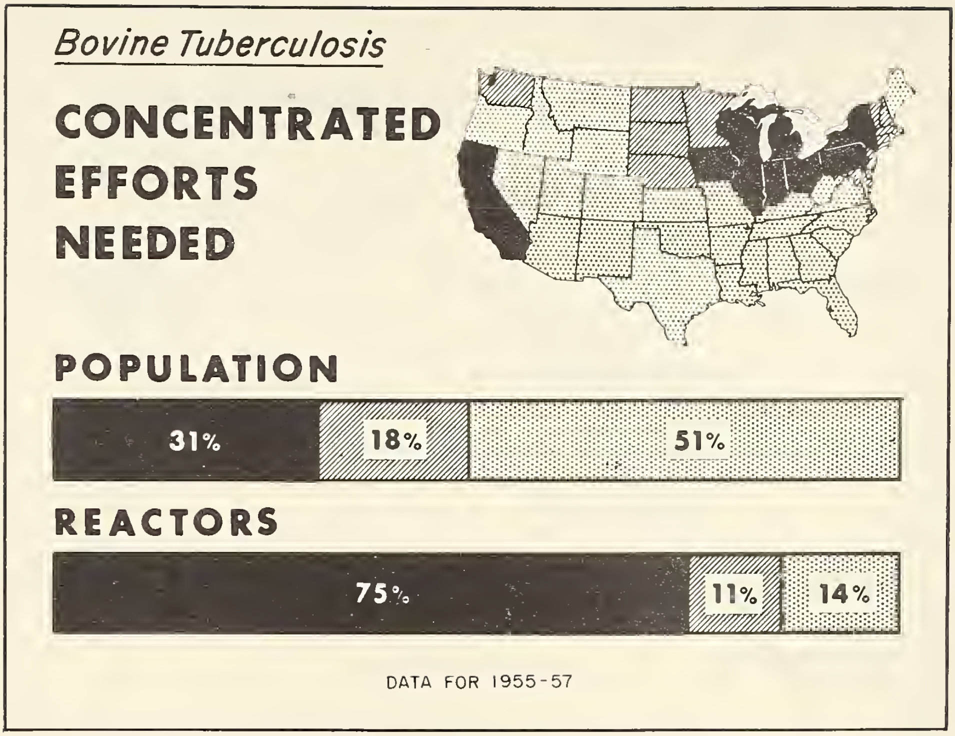


FIGURE 11 BN-9042

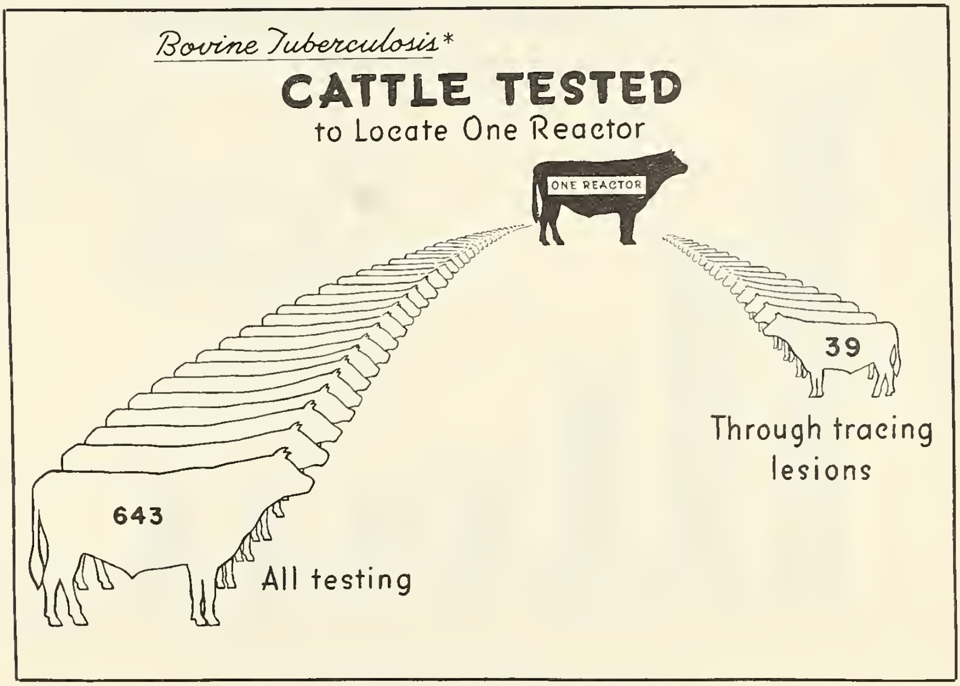


FIGURE 12 BN-9043

PRINCIPLES OF DISEASE ERADICATION

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Members of the conference: One develops a real good feeling when he comes back to college. For example, one thing I have noticed is that even when you give a speech here, the rostrum in this amphitheater is at a lower level than the audience.

After you leave college, you may make several public appearances and sometimes may feel that you're up on a pedestal. Often you stand at a level higher than the audience, and unfortunately some speakers address the audience so that their text is presented in that manner. So this room sets up a real good physical and psychological relationship between the speaker and his audience, and it probably comes closer to placing the speaker in proper perspective.

As far as glowing introductions are concerned, I heard a fellow from the Library of Congress introduced with a great elaborate introduction. I felt sorry for the fellow because he started out with the handicap of having to live up to a gigantic resumé of his accomplishments. The speaker handled it very well by saying, "One day, when I was riding in the car with my wife I said to her, 'Mary, do you know how few shoulders the destiny of this world rests upon?' She said, 'No, but I think it's one less than you think'."

Now, first of all, I'm to speak about the principles of eradication. As I stand here facing so many highly qualified men in this field, I suppose they wonder what in the world I am doing up here talking about the principles of eradication, especially since they were well identified years and years ago. However, I think this topic needs discussion. It does us good to review periodically any principles that we have, whether they are relative to our way of living or disease eradication. Careful review usually tells us how well we have adjusted to living with those principles and whether or not they were the principles we should have had in the first place.

One of the purposes of this conference is to at least have a representative in each State who has been exposed to the national problems in the eradication of tuberculosis in an endeavor to develop a uniform approach in handling the disease in each State.

That doesn't mean that when you return to your respective State you will say your program is all wrong and should be changed immediately. However, you will be able to determine how the program within your State may differ from the procedures that will be recommended here.

Perhaps some States are handling the situation better than others and you will be expected to bring this to the attention of those responsible for the national program. For those reasons, I am directing this report primarily to those individuals who have been selected from each State to attend this conference.

Before we speak of the principles, I think we should define what we mean by the term "eradication." In referring to the dictionary, I found this definition: "To pluck out by the roots something that has become established."

If you examine most veterinary texts on infectious diseases, you will find they discuss the great achievements of bovine tuberculosis eradication in the United States. I'm confused because according to the meaning of the word we haven't eradicated tuberculosis. In fact, we are here today trying to stimulate interest in its eradication. Unfortunately, there are many people who think that bovine tuberculosis cannot be eradicated. Now, if it cannot be done, let's quit kidding ourselves and others by talking about <u>eradication</u> when we mean <u>control</u>. But, if we really believe that it can be done, then let's roll up our sleeves and tighten our belts and get it eradicated.

One of the first questions that must be answered in any disease eradication program is, "What do we know about the disease?" Then, "Do we have all of the information necessary to carry out an eradication program?" The latter point is of extreme importance. It is probably one of the points that should receive the most consideration at this type conference. If we have all of the information to carry out an eradication program, then it should be full speed ahead. If we are lacking something, we should pinpoint these items and recommend them as immediate requirements for research.

Next, we should review the essential parts of the program and determine if they are sound from a disease eradication standpoint and practical.

Let's look at the features of the Tuberculosis Eradication Program. First, we know that we must have some method of determining how much infection we actually have. Usually, we rely on either a test, or clinical examination of animals to determine where a disease is and how much of it exists. In the Tuberculosis Eradication Program we have a reliable tuberculin test. Is this statement true? If so, fine; if not, what is wrong with it and what needs to be done about it?

How are the tests going to be applied, by whom, how often, and to what extent in each State, so that it will give us adequate

information relative to the actual incidence of the disease not for reaccreditation purposes but for eradication. Analyze it to determine what problems exist relative to this method of inspection and determine solutions to the problems. Following this, we must determine how effective our method of diagnosis is, such as our testing and laboratory confirmation procedures. If they are adequate, fine; but if they are not, we must crystallize those procedures that need modifying to give us the most efficient and accurate methods of diagnoses.

The program must contain measures of handling the disease once located, such as quarantine of infected and exposed animals on the premises. Afterward, the infected animals must be slaughtered and the premises must be cleaned and disinfected. Do we have any problems in this field, and if so, let's focus attention upon them.

In practically every disease that was eradicated in this country, there were people who said it could not be done. If someone said in 1951 that in order to eradicate vesicular exanthema we would have to get all the garbage cooked that was fed to hogs in the United States, the task would seem insurmountable. A review of the situation would have shown that in California the regulatory officials had been trying to get the garbage cooked within that State without success. Public health officials had for many years prior proclaimed that this method of feeding hogs was chiefly responsible for the incidence of trichinosis in people. They were doing their best to get the garbage cooked if it was fed to hogs, but less than one-half of 1 percent of the feeders were cooking it. Today, 7 years later, practically 97 percent of the garbage fed to swine in this country is being cooked.

In further discussions, we will note that one of the weaknesses in our program is the lack of a satisfactory trace-back of tuberculosis diseased animals. Yet, those working on the problem know that even though they have been unsuccessful, at times, in tracing back animals they are meeting with more success each year in successfully locating infection as a result of this procedure.

They say that the most emphatic method of getting a point across is to use the minimum amount of words and those that are most clear-cut. If you will pardon the expression, I will use the same word that the United States General used in the Battle of the Bulge when they asked him if he was ready to surrender. When people say that tuberculosis cannot be eradicated, I say "Nuts."

One of the most important essentials in any eradication program is industry, interest, and active support. We had that support because you can't reduce the incidence of a disease like tuberculosis to its present status without it. We lost it after we accredited States. For some reason, we settled for something short of what we actually wanted. Sure there are many who say that there is not an agricultural livestock interest in this country that will not say that bovine tuberculosis should be eradicated; but, this is not support. When the Russians put up Sputnik, it aroused the interest of the people of this country and they demanded that something be done by us, evidently regardless of cost. Now, I'm not saying that similar type pressure from the livestock industry is needed, but that is an example of what I mean by active interest and support. The most important challenge before us is to get back the interest and support of industry.

How can this be done? If we are going to continue to kid ourselves and others by talking about eradication when we mean accreditation, then I believe the support will continue to wane. If we actually take steps to eradicate the disease, the industry will give us their active support because I'm sure that they would be more than willing to buy complete eradication of this disease.

In summary, we have defined what we mean by eradication. We must keep a clear-cut understanding of what we mean by it. We should determine what measures we need, pinpoint the problems, come up with the solutions, establish a date for eradication, and strive for industry interest and support.

If you men have come here and are listening to the papers that are being presented with an attitude that the subjects being discussed are merely for review and not initially to stimulate action, then the conference will fail in its objective. If you came here to help identify the problems and aid in seeking their solutions, and even more important, to do something about it in your State, then we have taken the first major step toward bovine tuberculosis eradication within the past 15 years. The answer lies within each one of us.

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TUBERCULOSIS A NATIONAL PROBLEM

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St. Paul, Minn.

Tuberculosis of domestic animals is a problem of concern throughout the United States as well as most of the civilized world. It has been recognized as a national problem for at least 60 years. At the third annual meeting of the Interstate Association of Livestock Sanitary Boards, the parent organization of the United States Livestock Sanitary Association, held in Chicago in 1899, tuberculosis of cattle was the major subject of discussion. At that meeting, the late Dr. Leonard Pearson of Pennsylvania, introduced a resolution pertaining to this disease. Much of the wording of this resolution could be applied today. Section three of the resolution reads as follows: "While losses caused among cattle by this disease are large and sufficient to justify energetic effort to eradicate it, tuberculosis is also of much importance on account of the intimate relation of this disease of cattle to the public health."

Section six of this resolution reads: "This convention recommends that all States that have not already done so, shall authorize and empower the proper authorities to adopt well planned and conservative measures to repel the encroachments of this disease and to eradicate it where it is already established."

Note that the word "eradicate" appears in both sections quoted. It is clear from a study of these proceedings that livestock sanitary authorities at the turn of the century were much perturbed about the losses from bovine tuberculosis among cattle, as well as the danger it presented to public health. Also, even at that early date, it is evident that these agencies were considering measures for eradicating tuberculosis from the United States.

The magnitude of a campaign to eradicate a chronic disease already firmly established was, of course, tremendous. A number of years elapsed before an organized campaign for eradication which could give promise of success could be put into effect.

First, education of the public was necessary in order to support the program and secure the appropriation of adequate funds. It was also necessary to devise a satisfactory method of testing that would be less time consuming and expensive than the subcutaneous or temperature test used in the initial work in this country. Without the intradermal method, testing on the scale necessary for effectual eradication, could not be carried out.

Development and standardization of the intradermal test was accomplished late in the second decade of this century, and by 1923 was recognized and adopted in all States. By that time, the eradication of bovine tuberculosis under the area plan was well under way.

The testing of individual herds, particularly under the accredited herd plan, had been in operation since 1917, and had been widely adopted in all States. While this demonstrated the value and accuracy of the tuberculin test, there was still opposition in many quarters to the compulsory testing of all cattle under the area plan.

In some sections this opposition was pronounced. Some State and Federal officials, in order to overcome this opposition and establish and carry out the program, fell into a serious pitfall. Instead of selling the program on its merits, statements were too often made that when an area was declared modified accredited, cattle originating therein would be permitted to move freely to any part of the United States without restriction. Intentionally or not, this left the impression in many quarters that when a county or State had attained modified accredited status, the job was completed.

Most livestock sanitarians realized that modified accreditation was only the first plateau. However, few State and Federal veterinarians hammered home this idea. Many failed to stress the fact that attaining modified accreditation was only the first step, and that years of mopping up with a continuing need for further appropriations would certainly be necessary before eradication was complete.

In my opinion these assurances, regardless of how well meant at the time, probably contributed more than any other factor to the complacency of both cattle owners and veterinarians -- a complacency which we as livestock sanitarians now decry.

There are, of course, other factors that have helped to bring about this feeling of complacency. The vast reduction in the incidence of tuberculosis in itself has brought about the feeling by most livestock owners that tuberculosis no longer needs to be considered a serious menace.

In the last few years livestock sanitary officials and the veterinary profession in general have come to realize that further efforts will be necessary to complete the job of eradication. Most veterinary colleges are now demonstrating the technique of applying the tuberculin test and studying reactions obtained on previously sensitized animals.

During recent years, the need for careful application and observation of tuberculin tests has been emphasized by colleges and control agencies, but the unfortunate complacency of livestock owners, shippers, and legislative appropriating bodies is a most difficult matter to correct.

Regardless of how it occurred or who is to blame, the situation presently confronting livestock sanitary agencies is this:

1. Tuberculosis still exists to some extent in every State. This is a menace to the livestock industry and threatens to undo the tremendous progress we have already made toward eradication.

2. There is little understanding on the part of the livestock industry regarding this menace, and there is a feeling that much of the tuberculin testing now being carried out is an unnecessary and unreasonable expenditure of both private and public funds.

3. No material progress has been made toward complete eradication during the last 10 years, and in some areas there has been some increase in the incidence of this disease.

Faced with this situation, the question arises as to the steps which must be taken to finish the job we started 40 years ago. Dr. A. F. Ranney, Chief of the Tuberculosis Eradication Section, Animal Disease Eradication Division, of USDA, in his report on the status of Federal-State Cooperative Tuberculosis Eradication to the United States Livestock Sanitary Association in November 1957, has outlined certain steps that are essential to reactivate the eradication program. I would like to emphasize some of the points which he listed in his report:

1. Dr. Ranney stated that "We must reaffirm our confidence in the tuberculin test." This is of paramount importance. I believe, however, that the Uniform Methods and Rules of the United States Livestock Sanitary Association approved by the Agricultural Research Service, and the procedures followed in accordance therewith, are partly to blame for the lack of confidence in this well established test.

I believe it is entirely wrong to base the incidence of infection in an area on the number of reactors showing visible lesions rather than on those showing a positive reaction, whether or not lesions are disclosed on slaughter. I believe, too, that the form furnished by the Meat Inspection Division for reporting lesions could be worded to clearly indicate the animals are diseased, even when no visible lesions are found. At the present time owners of reacting cattle usually feel the animals were not diseased or the test was in error when they see a report which shows that the animal showed no visible lesions or was passed for food.

2. Dr. Ranney further emphasizes the necessity for more close attention to the need for proper quarantine of infected herds, and the need for supervision of the cleaning and disinfection of premises from which reacting animals have been removed. I am sure we must all agree with this view.

3. It is our experience in Minnesota that tuberculosis now appears where least expected. It is not common to find infection in herds previously infected which have passed the necessary negative tests and been released from quarantine. Instead infection is being found in previously clean herds. For that reason we believe systematic testing of all cattle at definite intervals must continue as a primary activity in tuberculosis eradication.

It is entirely possible that the period of accreditation could be lengthened when the percentage of infection reaches the vanishing point, but in my opinion many years should elapse before periodic testing of all cattle in an area can be eliminated as the principal method of eradication.

4. If we are to reach our goal of complete eradication, it seems essential that some clearly stated objective should be established. Great progress was made when we had modified accreditation as a goal to shoot at. Whether there should be an intermediate stage between modified accreditation and an area completely free from tuberculosis, I am not sure. It would seem, however, that we have now reached the stage where we should strive to attain tuberculosis-free areas and that such areas should be clearly designated.

To encourage attainment of such status, uniform methods and rules should be devised whereby livestock owners might profit substantially through the recognition of a higher status for animals originating in such area. Since at the present time the highest standard officially obtainable is the modified accredited status, there is little incentive to create enthusiasm among livestock owners and veterinarians toward a reactivated eradication program.

It must be recognized, however, that such a status would again involve further restrictions on the importation of cattle from areas which have not met the higher classification, which presents a tremendous problem because of the ever increasing movement of cattle from one part of the country to another. This problem would be particularly important in areas where cattle feeding is one of the principal activities of the livestock industry.

There is another problem which must be faced if we are to attain complete eradication. This problem involves the differences that exist between different States and different sections of the United States. Disease eradication is a State problem, and because these differences do exist it should remain so.

Federal agencies have been and can be of tremendous assistance in establishing certain standards that must be met for recognition, but the methods of attaining these standards must be determined by the State. State regulatory officials are necessarily guided by State laws and appropriations, as well as by the prevailing methods employed in their respective States.

Procedures that are practical in Minnesota, for instance, might not work in Wyoming or Mississippi. Even the attitude of the public toward State or Federal control differs in different areas, and must be considered in the establishment of a State program.

In addition to the establishment of standards by the Federal Government, Federal money has been of tremendous help to all States in achieving and maintaining modified accredited status. This money should not, however, be employed by the Federal Government as a means of forcing any State to adopt methods which in the opinion of State officials are not appropriate. Instead, this money should be used to assist the States in carrying out their own programs in any way which gives promise of attaining the standards that have been established.

Tuberculosis is and has been both a State and national problem for more than 60 years. And although tremendous progress was made until all of the 48 States attained a modified accredited status, since that time, there has been a let-up in the efforts of all concerned to complete the job of final eradication.

In order to reactivate the program, it is essential that we overcome the complacency now existing by establishing higher standards, educating the public to meet such standards, and devising methods whereby an area which has attained complete eradication can be properly recognized.

HISTORY OF TUBERCULIN AND TUBERCULIN TESTS AND THEIR RELATIONSHIP TO THE DIAGNOSIS OF TUBERCULOSIS

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Tuberculin Is One of the Best Diagnostic Tools Yet Prepared by Man!! Before the large-scale production of tuberculin with synthetic media by the United States Department of Agriculture in 1933, testing of cattle and other animals was carried out with tuberculin made essentially in the same manner as the original product by Robert Koch more than 65 years ago.

It is true that during the years that have elapsed since Koch's original announcement, many different forms of tuberculin have been proposed for use in both veterinary and human medicine. Many of these products were intended for use in the treatment of cases of human tuberculosis. Koch himself proposed such preparations, which were made by grinding and extracting components of *Mycobacterium*. Tuberculin prepared by growing *Mycobacterium* on synthetic culture media was used in human medicine, and on occasion in veterinary medicine, for treatment. However, no form or modification of Koch's old tuberculin has been used in such large quantities and with such outstanding results as that made in synthetic media by the USDA.

There was no question of the remarkable efficiency of the Old Tuberculin of Koch. It enabled us to reduce bovine tuberculosis in the United States between 1917 and 1932 to a fraction of its early prevalence. In 13 States, the disease was decreased to a point where it ceased to exist as a menance to the dairy industry and to the public health. However, it must be stated that this, like other biological tests, is not perfect.

There is a small percentage of instances where it has not been possible to find lesions of tuberculosis in reacting cattle, or where tuberculous animals have failed to react on a single test. Research has continued with the objective of reducing this small percentage of possible error and of developing other tests.

KOCH'S OLD TUBERCULIN. In order that the differences between the synthetic tuberculin, which has been used exclusively in eradication programs since 1933, and the Old Tuberculin of Koch may be made quite clear perhaps we should first describe very briefly the Koch method of producing tuberculin.

A clear broth is prepared by extracting lean beef or veal with water. To this, 1 percent of peptone is added. The crude peptone is obtained by subjecting either meat or the casein of milk to partial peptic digestion so that it consists of a mixture of proteins. To the broth containing peptone, there are added 0.5 percent of sodium chloride and from 4 to 7 percent of glycerin. The mixture, which is generally referred to as glycerinated broth, is put in flasks, sterilized, and inoculated with pure cultures of the *M. tuberculosis*. In some laboratories the bovine type is used, but in the United States the human type is used.

The bacteria grow on the surface of the broth, forming a film or pellicle that gradually covers the entire surface in about 6 to 8 weeks. The *M. tuberculosis* grows actively on such a broth for only a few weeks. At the end of approximately 2 months, broth cultures of the *Mycobacterium* are sterilized and the dead bacilli are removed by filtration.

A clear, sterile filtrate, concentrated to a desired strength and containing a suitable preservative, constitutes the tuberculin that was used for testing cattle in the United States.

All of the Old Tuberculin produced by this method by the USDA was concentrated in such a manner that the final product contained 40 percent of the original volume of the culture fluid. And all the Old Tuberculin produced and used by the USDA for the intradermic test contained 10 cc. of Old Tuberculin in each 40 cc. of the final product, or 25 percent by volume.

It is, therefore, evident that the final product used for testing cattle contained not only the suitable substances derived from the growth

of the tuberculosis organism on broth, but also any portions of the culture medium that had not been used up during the growth of the *Mycobacterium*.

It was generally understood that the composition of the Old Tuberculin was extremely complex. It always contained considerable quantities of unused glycerin. In addition, there were present unused nitrogenous substances derived from the beef, as well as similar nitrogenous protein materials derived from the peptone which is added to the broth.

THE SYNTHETIC MEDIUM. Chemists and veterinarians working for the USDA conducted detailed studies for many years in an effort to devise an entirely synthetic medium for the growth of the *M. tuberculosis*. It was in the early 1930's that this synthetic medium was made possible by the continuing research of the Department. The synthetic medium constituents are asparagin, dipotasium phosphate, sodium citrate, magnesium sulfate, ferric citrate, dextrose, and glycerin.

Since the early 1930's, this simple synthetic medium has been used internationally for growing *Mycobacterium*, the product of which has become known as synthetic tuberculin. This tuberculin has been more uniform and more specific than Old Tuberculin.

The following three facts are very worthy of note:

(1) The growth of *Mycobacterium* is three or four times more abundant on the synthetic than on the old broth medium;

(2) The proteins of the synthetic culture filtrates are derived entirely from the *Mycobacterium*; and

(3) The constituents in the synthetic medium are entirely used except for a small amount of mineral salts and a trace of glycerin.

Many investigators have claimed, and it has been conclusively shown by the research of Long and Seibert, that the active substance in synthetic tuberculin is a protein derived from the *M. tuberculosis*.

Since the cultures on the synthetic medium contained no protein except that derived from the *Mycobacterium*, and since the growth of the *Mycobacterium* was very luxuiant, it seemed probable that the tuberculin prepared from such cultures might be not only more potent but also more selective and less likely to result in nonspecific reactions than the Old Tuberculin of Koch.

Many tests have been conducted over a considerable period of years in standardizing synthetic tuberculin and comparing synthetic tuberculin with the Old Tuberculin. It has not been possible to detect any significant differences in the reactions obtained in cattle when synthetic

tuberculin of full strength and one diluted 25 times is used but differences are detectable with one diluted 50 times.

While this may seem to be a rather crude significance test, this degree of accuracy has proved to be biologically sound. For details of comparative test on cattle with synthetic tuberculin and Old Tuberculin, reference is made to Dr. Dorset's paper published in the Proceedings of the 37th Annual Meeting of the United States Livestock Sanitary Association in December, 1933.

The tuberculin reaction is generally accepted as a phenomenon of delayed hypersensitivity or allergy due to the sensitization of the body tissues to the products of growth of the mycobacteria. The reaction may be either systemic or local, depending on the way in which tuberculin is applied to the tissues of responsive animals. When tuberculin is injected subcutaneously, it produces a local lesion at the site of injection and a systemic reaction which consists of fever and general symptoms of intoxication, and occasionally death.

Experience has established the highly specific nature of the tuberculin reaction. It is recognized, of course, that every case of tuberculosis, either in man or in lower animals, will not necessarily give a positive reaction to tuberculin and, conversely, positive reactions are occasionally observed in apparently healthy persons and cattle. Because of the inadequacies of macroscopic and microscopic methods of detecting the presences of tuberculosis, we tend to infer inefficiencies of the tuberculin tests.

The subcutaneous test was the one most extensively used in this country and in certain continental countries, but has been almost entirely superseded by the intradermal test for official purposes in those countries in which a serious attempt has been made to control tuberculosis in cattle.

The ophthalmic, or conjunctival, tuberculin test of Wolff-Eisner, Calmette, and Guerin has been discarded for use in man owing to the severity of the reactions which it sometimes produces. However, the test is still employed in cattle to a limited extent. In practice, the test has not proved significantly reliable to warrant its use alone. Nevertheless, it is used occasionally in conjunction with some other method.

During the past three or four decades, considerable use has been made and value shown on the intradermal test for detection of tuberculous infection. It was shown by Von Behring in 1899 that the skin of a tuberculous bovine was responsive to tuberculin, and since that time various methods of applying the intradermal test have been employed.

The value of the intradermal test in providing clear-cut evidence of allergy to tuberculosis was plainly demonstrated by Moussu and Mantoux

(1908), who described the type of response which might be expected in tuberculous and nontuberculous animals. Since the reactions to the intradermal test can be read with a considerable degree of accuracy, the method has been in great favor for 30 years or more, and has practically replaced the subcutaneous test.

The techniques of Christiansen and Stubb (1910) consisted of introducing concentrated tuberculin into the deeper layers of the dermis. An area on the side of the neck was prepared, and a preliminary dose of 0.1 cc. was injected into a fold of the skin. At the 48th hour, a positive response in the form of a soft edematous swelling resulted. However, if the reaction was in the form of a hard circumscribed swelling, which characterizes a negative reaction, a second dose of 0.1 cc. was introduced into the center of the primary swelling.

Investigations of Buxton and McNaulty (1928) seemed to indicate that this procedure considerably assisted in the detection of tuberculous infections in all its forms. This did not prove to be the case, and consequently the procedure has been discarded.

The Stormont test was developed in Northern Ireland by Kerr, Lamont, and McGirr. It involves two intradermic injections in the same position at 7-day intervals. These injections were made in the cervical area. The second injection was observed in 24 hours, and an increase in skin thickness of at least 5 mm. more than that caused by the first injection constituted a specific reaction.

The intradermic caudal fold test, intradermic vulva test, and the intradermic cervical test are all further variations in the use of intradermal testing procedure.

The ophthalmic test is still another test which has, over the years, received considerable attention. It is usually conducted as follows: A sensitizing dose of tuberculin or a disk is installed underneath the eyelid of the animal. After an interval of 72 hours, a second dose of tuberculin or a disk is placed in the same eye. The disks usually contain twice the regular intradermic strength of tuberculin.

Four readings are made at 2-hour intervals after the installation of the second disk. A positive reaction is indicated by copious lacrimal secretion, usually mucopurulent in an extreme reaction. It is reasonable to suppose that the hypersensitivity which develops in the tissues as a result of the invasion of M. tuberculosis manifests itself in a similar manner in all infected subjects, but it should be recognized that there are slight differences in the allergic response of different species.

While there is no reason to believe that there are any significant qualitative differences in the results of the intradermal test in the various infected species, there are quantitative differences of skin sensitivity.

Attention may be drawn to certain peculiarities of the intracutaneous tuberculin test in cattle since some interesting differences have been observed in the bovine subject as compared with man. The comparatively large doses are required to detect all infected cattle, some of which are only slightly sensitized. This is in marked contrast to the appreciably smaller amounts needed to reveal tuberculous allergy in man. Although this difference may be dependent in part upon the relative thickness of bovine skin, which ranges from 3 to 12 or 15 mm., it is unlikely that this factor is entirely responsible for the relatively lower degree of sensitivity in cattle.

Another possibility is that the cutaneous tissues in the bovine subject are less responsive than those in man. Cutaneous reactions in man are frequently obtainable with tuberculin diluted 1:1,000 or more. Similar responses can be observed in guinea pigs at the appropriate stage of tuberculosis, whereas in cattle it is usually necessary to employ concentrated tuberculin.

Although hypersensitivity does not occur frequently in tuberculous cattle, positive reactions of 40-50 mm. may be induced in them at the time of maximum sensitivity with dilutions of 1:100, or even 1:1,000, of regular tuberculin. On the other hand, in other cattle with less sensitivity, 0.1 cc. of undiluted tuberculin is required to produce a reaction of equal size. Consequently, the response to concentrated tuberculin in a large proportion of the reactors in an affected herd is of moderate intensity.

Because the recommendations are particularly pertinent in view of our current tuberculosis problems, I would like to repeat some points from the report presented by the committee of tuberculosis at the 49th annual meeting of the United States Livestock Sanitary Association, held in December, 1945.

"1. In the Report of the Committee on Tuberculosis for 1944 it was recorded that Federal regulations were being contemplated to correct certain weaknesses in the existing regulations governing the importation of cattle for purposes other than immediate slaughter. The Committee notes with much satisfaction that the necessary regulatory changes were drafted and became effective on and after February 1, 1945 (B.A.I. Order 379).

"2. In the report for 1944 the Committee on Tuberculosis expressed skepticism regarding the policy followed in certain areas of the United States whereby only a small percentage of the herds are retested annually. As a result of this practice many herds have not been retested for as long as twelve years.

"The Committee reiterates its disapproval of this, a policy which if persisted in can lead only to serious consequences. The Committee is of

the opinion that long intervals of time between retests has in some areas resulted in an increase in the incidence of tuberculosis, and strongly urges that the situation be corrected as soon as possible....

"3. During the entire history of the testing of cattle with tuberculin, one of the most perplexing problems has been that created by the animal that reacts positively to a diagnostic dose of tuberculin but in which confirmatory evidence of tuberculous infection cannot be established. To those who believe the specificity of tuberculin to be infallible, the failure to find lesions of tuberculosis in an animal that had reacted to tuberculin is due to the fact that the search was not sufficiently complete, or that the infection was in the incipient stage.

"An honest approach to this problem requires that we admit that experience of the past twenty-five years incites in the minds of many a reasonable doubt as to whether or not tuberculin is a diagnostic substance of absolute specificity. While we are familiar with the many ideas that have been advanced in explanation of the nonvisible lesion reactor, candor requires that we admit that at the present time there are no explanations supported by an adequate amount of evidence.

"The Committee does not wish to weaken confidence in tuberculin as a substance of tremendous and proved value in detecting tuberculous infections. By its use, man's greatest conquest over tuberculosis has been accomplished. We must however recognize that at the present time a very high percentage of cattle reacting to tuberculin are without other demonstrable evidence of infection with tubercle bacilli.

"If agents other than tubercle bacilli are capable of sensitizing cattle to tuberculin, one must accept the fact that even though tuberculosis be eliminated entirely from the herds of this country a considerable percentage will continue indefinitely to react to tuberculin.

"If progress in the solution of this problem is to be made we must maintain an open-minded attitude. To insist without confirmatory evidence that a positive reaction to tuberculin is unequivocal proof of the presence of a tuberculous infection is prejudicial to the best interests of all who are seriously concerned with this perplexing situation.

"The answer to the question 'can cattle be sensitized naturally to a diagnostic dose of tuberculin by agents other than tubercle bacilli?' can only be secured by research and more research. Therefore the Committee strongly recommends that investigators be urged to explore this problem, and where work is contemplated that adequate funds and competent personnel be provided to insure a thoroughly satisfactory investigation.

"The answer to the question previously stated would be welcomed by cattle owners and control officials alike and would enhance the confidence so essential to the continued success of the tuberculosis eradication program, the primary objective of which is to detect and eliminate from the herd those animals infected with tubercle bacilli....

"4. With the marked reduction of the incidence of tuberculosis in cattle, and the general acceptance of pasteurization as an effective safeguard in the production of a safe milk supply there is likely to be an undesirable tendency to forget that bovine tubercle bacilli are capable of producing in man every variety of tuberculosis of which the human type of the bacilli is capable.

"It is perhaps useful occasionally to review briefly the pertinent facts concerning the transmissibility of bovine tubercle bacilli to human beings. These facts are (1) Incomplete data from investigators in different parts of the world indicate that approximately 10 percent of tuberculous infections in man were due to the bovine type of the organisms. Therefore the organism of cattle tuberculosis must be considered an important pathogen for human beings; (2) The highest incidence of bovine type of infection in man occurs in Great Britain, with Denmark next in order of frequency; (3) Children are more commonly affected by the bovine type of the organism than are adults, the highest incidence of infection occurring in children under five years of age; (4) The usual portal of entry of bovine tubercle bacillus in human beings is the alimentary canal; (5) While most of the reported cases of bovine tuberculosis infection have been extrapulmonary in character, several hundred cases of pulmonary tuberculosis in man due to bovine tubercle bacilli have been recorded; (6) The transmissibility of the bovine type of infection from man to cattle has been established; (7) The possibility of the transmission of bovine tubercle bacilli from one person to another is impressive, especially from persons with pulmonary tuberculosis of the bovine type; and (8) There is no reason for believing that the bovine type of the tubercle bacillus is less virulent for human beings than is the human type of the organism.

"The foregoing constitute sufficient evidence to justify the conclusion that tuberculous cattle are a serious menace to human health and should not be tolerated by an informed society. It follows, therefore, that no laxity be tolerated which will make less effective the methods or policies designated to control and eradicate the disease.

"5. While the seriousness of infection due to the avian tubercle bacillus has been generally recognized for many years, the problem remains. To quote from the report of the Committee on Tuberculosis for 1944 -- 'The measures designed to reduce or satisfactorily control the disease in those sections of the United States where it is rampant have not, in our opinion, been effective.'

"In many areas avian tuberculosis is one of the major diseases of poultry. Furthermore the bacillus of avian tuberculosis is capable of infecting other species of livestock. Therefore we recommend that the methods now being followed in the attempt to control avian tuberculosis be subjected to a critical examination by a special subcommittee charged with the responsibility of obtaining an accurate and comprehensive understanding of the situation and to formulate plans for an effective attack against the disease."

OUR PRESENT TUBERCULIN

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The tuberculin test has been used in detecting tuberculosis in cattle since the early days of the discovery of tuberculin by Robert Koch in 1891. Its accuracy has stood the test of time and usage as one of our most reliable diagnostic reagents in animals. As early as March 31, 1892, tuberculin was employed to test a herd of cattle in Pennsylvania by Dr. Leonard Pearson using tuberculin that he brought from Europe.

The former Bureau of Animal Industry undertook work on tuberculin in 1892, and began to supply the product to State and Federal veterinarians for field use. There was immediate interest in the use of the product for detecting tuberculosis and the demand for it steadily grew. In the year ending June 30, 1906, about 100,000 doses were prepared and distributed. During the twelve-month period ending June 30, 1959, approximately 10,000,000 doses will have been prepared and distributed.

Along with the program to produce tuberculin for field distribution, a very active research program involving chemical and biological studies of tuberculins was also undertaken very early by the former Bureau of Animal Industry. As this research work progressed over a period of many years the Bureau was recognized as the foremost source of information relating to the production and testing of tuberculins in the United States. Most of the other laboratories working in this field in all parts of the world depended on the Bureau to provide them with standardized materials for checking and improving their own products.

Dr. Marion Dorset, former Chief of the Biochemic Division of the Bureau of Animal Industry, first selected the three strains of Mycobacterium tuberculosis (Pn, C, and DT) that are now used worldwide for the production of tuberculin for both animal and human use. Dr. Dorset isolated these cultures from tuberculous children in Washington, D. C., about 1903. Another significant contribution of the Bureau of Animal Industry was the development of a synthetic medium for the production of tuberculin in 1934. This medium provided a tuberculin of much higher sensitivity and purity as compared to the old tuberculin produced on non-synthetic mediums. In 1934 the preparation of the old type of tuberculin was discontinued in the United States, and the synthetic medium accepted as the standard. Many other countries adopted the use of this medium as first developed by the Bureau of Animal Industry and at the present time most tuberculins are produced on the synthetic medium of the BAI.

Cultures are grown on the above medium at a temperature of 37.5° C. for 10 weeks. The average maximum weight of bacteria, which is usually reached before the end of the seventh week, is approximately 2 grams (dry weight) per 100 ml. of medium. When the cultures have made their full growth they will have used up practically all the constituents of the medium. At the end of the growth period the cultures are sterilized in flowing steam for 3 hours to kill the tubercle bacilli. After being cooled, the sterilized cultures are strained through gauze. The filtrate containing the active principle of tuberculin is evaporated to slightly less than one-fifth of the original volume of the culture medium. Glycerin and phenol are added in equal quantity bringing the total volume to 40 per cent of the original volume of the culture medium. Finally the product is filtered and passed through high speed centrifuges until clear and free of all traces of tubercle bacilli.

In 1955 after more than 60 years of experience in preparing various types of tuberculins, the ARS discontinued activity in this field. This action was necessary due to the lack of adequate facilities for working with tuberculosis cultures. Consequently, a commercial source of the product was developed through contract arrangements under which every stage of tuberculin production is constantly under close supervision by trained ARS personnel. Each step to be followed in production is closely checked and all the procedures used in production are those developed and used by the ARS. Persons associated for many years in the development and production of tuberculin by the Bureau of Animal Industry presently serve as consultants in the production program, and earlier provided the information on which are based our production and testing standards. If at any time questions arise regarding the production of tuberculin obtained from commercial sources, these consultants are available for discussion of the problem and their recommendations are closely followed. ARS research personnel who have spent many years working in this field are also constantly available to advise us regarding questions that arise in the fields of tuberculin production and evaluation. These practices have insured us of a product of highest quality and potency for use in field programs.

In addition to providing detailed specifications on the production of tuberculin, government supervision includes the use of specific biological and chemical tests by both ARS laboratories at Beltsville and by the producing firm before the product is released for distribution. ARS biological tests include comparison of the commercially produced product with a previously selected standard produced by ARS, using guinea pigs that have been sensitized with cultures of the tuberculosis organism. Test results with the ARS product must compare very closely with those obtained with the commercially produced product. All of the data derived from these sensitivity tests in guinea pigs is subjected to statistical analysis

and the final disposition of the product is dependent upon the results obtained. Chemical tests are also conducted to determine the total nitrogen in the product and the nitrogen precipitable by trichloracetic acid. These determinations provide information on the amount of active principle in the product. The acetic acid precipitation test which has been employed by the Bureau of Animal Industry for many years for standardizing and checking tuberculins provides additional information on the amount of active principle in the product. Chemical tests also include those for the level of phenol in tuberculin and the determination of its hydrogen ion concentration.

It has been pointed out by those using tuberculin under field conditions that the commercial product is slightly less dark in color than was the ARS product distributed prior to 1955. This difference in color has no relationship to the potency or quality of the tuberculin and is due to the fact that the commercial producer prefers to filter the dextrose solution prior to its addition to the medium. This procedure precludes the heating of the dextrose and results in a lighter color of the finished product since dextrose upon exposure to heat becomes carmelized and a darker color is formed. It was the practice of ARS in producing tuberculin to add the dextrose to the medium before heating rather than to employ the procedure of filtering the solution before addition to the medium. This matter was thoroughly considered at the time a contract was drawn up for tuberculin production and it was determined that the addition of the unheated dextrose would in no way alter the potency or quality of the finished tuberculin.

In an effort to accumulate data on the relative sensitivity of ARS-produced tuberculin and that produced under contract, the ARS has undertaken comparative experiments to test the relative sensitivity of the two tuberculins on cattle under field conditions. Herds of cattle for the experimental study were carefully selected on the basis of past history of tuberculosis, and the reactions obtained with the two products were correlated with the findings on post mortem as far as possible. A total of 585 animals on 13 premises in 4 States were represented in the study. Five hundred and fifty-two of the total animals tested were negative to both tuberculins. Contract tuberculin representative of six serials was included in the study. Of a total of 33 animals which reacted to some degree to both tuberculins, in no case did the commercial product detect any reacting animals which were not detected by the ARS product. Neither did the ARS product detect any animals that were not detected by the commercial tuberculin. Reactions to the two tuberculins were quite comparable. Deviations when noted were slight. These comparisons were based on allergic reactions of caudal and vulval tissues.

Results did not indicate more NGL reactors with commercially produced tuberculin than with the ARS product. When suspicious reactors were encountered, the degree of reactions was essentially equal whether ARS or commercially produced tuberculin was used. These results indicate that the various lots of the commercially produced tuberculin and the ARS standard

react in a very comparable manner under practical field conditions when used to test cattle. Present plans are to extend the comparative tests to new serial lots of contract tuberculin as it is received by our laboratory.

In an effort to develop more detailed information on factors causing reactions to tuberculin in no-gross-lesion cases under field conditions, the ADE has established an investigational project on tuberculosis at the Ames Interim Diagnostic Laboratory. The program of this unit will include detailed laboratory studies of specimens collected from animals revealing NGL reactions. It is hoped that this work will provide additional data on the cause of some of the NGL problems occurring in the field. It is well known that in the field of human tuberculosis many new types of bacterial organisms closely resembling Mycobacterium tuberculosis are being recovered from patients thought to be tubercular. In maintaining the confidence which has been built up in the tuberculin test over a period of many years, it is important to develop newer information on some of the causes of NGL reactions as they are encountered in the field. With the establishment of the new Ames National Animal Disease Laboratory we will be in a better position to expand this work on the experimental study of tissues derived from animals reacting to the tuberculosis test in the field and to undertake expanded research programs on tuberculosis and tuberculin.

The validity of the tuberculin test had been demonstrated by scientists in all parts of the world over a period of many years. Our present tuberculin continues to provide us with one of the most valuable diagnostic agents available to man for the detection of disease. The high standards set for the product in the past will be continued in the future.

THE GENERAL PRACTITIONERS' RESPONSIBILITY IN TUBERCULOSIS ERADICATION

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The general practitioner has a definite responsibility to his clients in all phases of animal husbandry. Located as he is, either in a small town or rural area, he is regarded not only as their veterinarian, but also as a friend and advisor regarding their herd problems.

I believe that the veterinarian who takes an active part in the Federal and State tuberculosis program is doing his government, his community and his clients a real service. Many herd owners have a mistrust of the "outsider" who comes in to test his herd, seeming to harbor the idea that he is there to harm rather than help them. However, if they are aware that their own veterinarian, whom they have faith in, is taking part in this program, their cooperation is practically assured.

I have been a practicing veterinarian in Arenac and Bay Counties for over 25 years, and have participated in State and Federal testing throughout these years. In fact, in my early years in practice the program was the deciding factor in my remaining in practice in this area, for without its economic aid I would have had to give up.

In my years of testing I have never had anyone refuse to allow me to test his herd. True, I have had some skeptics, but after a sincere discussion they have been willing to give their permission. I believe only the practicing veterinarian can give the assurance that is needed in these cases.

I could give many instances from my experiences, which to you may seem foolish, but many have one common underlying factor -- negligence or carelessness on the part of someone in the testing program.

Some of the stories told to me by owners may be of interest here. One owner told me that I could do the testing if I disinfected my boots (which I always do) because the last tester didn't and right afterward his cows all had flu. Another one insisted on supervising the amount of tuberculin in the injection because the last tester put a lot in the first cow and it reacted and the ones where he just used a little didn't react.

Still another claimed that the last time the tester got in the pen to test a bunch of loose cattle he missed two or three. When he came back to read the test he let them run through the door and passed them all even though the owner claimed he had checked them the night before and had found two animals with noticeable swellings.

Most of these misunderstandings could be avoided if standarized procedures were worked out. Such, I understand, is the purpose of this conference, and I am very happy that as practicing veterinarians we have an opportunity to participate in the drafting of these procedures.

It is true that accredited veterinarians could not assume responsibility for all program testing due to the fact that such testing, when assigned, must be completed in a reasonable length of time. However, I feel that the veterinarian has a responsibility to the program and to his clients to take an active part in testing."

The veterinarian who shrugs his shoulders and complains that he hasn't the time, or the job doesn't pay enough, is giving a "black eye" to the testing program. In the long run he is also depriving himself of an excellent opportunity to make new friends and develop new business.

Over the years I have found that I must keep myself informed of all that is best for my clients' herds. When I know that something is good for them it is my responsibility to sell it to them and there is no better way to sell it than to be part of it. That is why I think that a large animal practioner should take part in these programs as much as his time will allow.

VETERINARY COLLEGE COOPERATION IN REGULATORY PROGRAMS

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The title of my presentation contains the word, "cooperation." It is a pity that we don't have a new, more descriptive word. "Cooperation" has been used so much, and misused so often, particularly in diplomatic circles, that it has become for many people an almost meaningless cliche. But for our discussion, let us consider that it has been at least temporarily restored to its original, dynamic connotation.

I have been convinced for some time that the natural tendency of all reasonable men is to cooperate with those whom they understand. I am persuaded furthermore that communication fosters mutual understanding and, therefore, that cooperation will almost invariably follow adequate communication. So our principal concern is to improve and sustain communications between all the agencies concerned with animal disease control. In doing this we will virtually assure cooperation. And in saying this I probably have put the whole point of my speech into a few words. But rather than stop at this point, which probably is what a really wise speaker would do, let me elaborate just a little on this matter of better cooperation through better communication.

Much of the world's waste, distrust, and failure can be blamed on breakdowns in communications. A prominent industrial executive recently made the startling statement that if a certain contemplated research will cost less than $100,000, it is cheaper to go ahead and do it than to search our disorganized scientific literature to see whether it has already been done by someone else! It has been estimated that up to 85 percent of the average research worker's time is wasted because of inadequate communications with other workers in the same subject-matter field. For a recent example of distrust engendered by lack of understanding the poor communications, consider the ill-fated good-will tour of Vice-President Nixon to South America. And one of modern history's classic examples of communications failure is the decimation and subjugation of China, first by Japan and then by Russia -- not purely by force of arms or numbers of troops, but largely because the Chinese people were disorganized and, speaking hundreds of different dialects, could not even communicate effectively with each other.

If the colleges are kept informed about the animal disease regulatory programs and if, in turn, regulatory workers are kept informed about the work of the colleges, especially their research and diagnostic services, cooperation naturally follows because it becomes so obvious that there are great mutual benefits. There are many ways in which this desirable communication can be maintained.

Explaining regulatory programs to veterinary students. Most veterinary colleges arrange for federal and state animal disease control workers

to meet with their students and acquaint them with this important area of the profession. All of the colleges presumably show their students the numerous movie films on animal disease control which are available, usually through the Agricultural Extension Service.

A valuable way to inform the veterinary student about regulatory programs is to arrange for him to visit regulatory workers on their jobs -- to actually see the programs in action and, if possible, to participate temporarily in them. Possibilities are almost limitless here if the college is not too far from centers of regulatory activity and if both college and regulatory officials recognize the importance of joining forces to provide the best possible training for these future veterinarians.

The College of Veterinary Medicine at the Ohio State University has been the leader in this development. No other veterinary college provides so much on-the-job training in all aspects of veterinary public health and regulatory work. And it is safe to say that the graduates of no other veterinary college are so well prepared to serve effectively in these vital and expanding veterinary activities.

Of course Ohio State has the advantage of location within a large, capital city, close to Federal, State and municipal health and livestock regulatory offices. But a number of other colleges share in some degree this kind of an advantage, yet they have not developed similar programs. Some have ventured the observation that Ohio State may be ahead of the times with her program. I suspect that it would be more accurate so say that the rest of us are behind the times.

<u>Keeping regulatory personnel informed of college activities and problems</u>. Communication and cooperation are "two-way" words. Consequently fullest cooperation between college and regulatory agencies can be expected only if regulatory workers are kept up-to-date on activities of college staff members in related subject matter fields.

Regulatory personnel stationed nearby should be made welcome and encouraged to visit the campus frequently. In many institutions it is possible to give them temporary academic appointments, or to officially designate them as consultants, thus giving them some status on the campus, making them feel more welcome, and qualifying them for special privileges such as use of the library, access to certain laboratories -- even a higher priority for the purchase of football tickets.!

For those regulatory workers in other parts of the State, extension veterinarians can serve effectively to keep them posted on what is going on at the college, particularly in research. And, of course, occasionally these workers can be assembled at the college for a mutual exchange of information. In other words, we can do at the State level--and more frequently -- the kind of thing we are doing at the Federal level at this conference.

The animal disease reporting service. The hub of the whole regulatory program logically should be an adequate, accurate, well-supported animal disease reporting service.

How can the State efficiently plan its regulatory program if it doesn't know what diseases most widely or seriously afflict its livestock? How can research dollars be wisely spent if we do not know what our most important animal disease problems are? How can a developing epizootic or an introduced exotic disease be nipped in the bud if no record is made of its presence and distribution?

How will we know where to place the emphasis in our clinical teaching if we do not know which diseases are most important in our State? The disease reporting service is central to all these activities. It is our most important single agent of communication. And it deserves far better support than it receives in most States.

The veterinary diagnostic service. There is wide variation among the States in the level of development of their animal disease diagnostic services. Like the reporting service, an efficient diagnostic service is essential to an effective animal disease control program.

The most dependable information on the animal disease report is that which comes from the diagnostic laboratory. Furthermore, most important research problems are first turned up in the diagnostic laboratory. And outbreaks of rare, new or exotic diseases are more likely to be identified by the diagnostic laboratory than by the private practitioner because of his lack of facilities. Yet in many States the veterinary diagnostic service, like the reporting service, is a stepchild which survives on budgetary scraps if at all.

In many, perhaps most, of the States, the bulk of laboratory veterinary diagnostic work is done at the veterinary college or the department of veterinary science of the land grant university. Too often no budget exists for this service and, consequently, it is done by veterinary personnel out of interest, kindness, or resignation, and often after regular hours. Not only is such diagnostic work frequently superficial, even inaccurate, but those who submit the specimens are dissatisfied with the delay in receiving reports.

In some States, fairly adequate diagnostic facilities exist but these are so widely scattered and so poorly coordinated that little benefit is derived from them for the teaching, research, extension, and regulatory programs.

In other States better consolidation of diagnostic facilities is accomplished by placing them under the control of the agricultural experiment station. However, money is appropriated to experiment stations for research and wherever research and diagnostic service are combined, service soon becomes the tail which wags the research dog.

The logical solution to this dilemma is a central animal disease diagnostic laboratory, supported by a separate budget, and staffed by competent specialists who can devote their full time to diagnostic problems. Such a laboratory should be located as close as possible to the veterinary college or veterinary science department and under its administration to facilitate coordination with the teaching, research, and extension programs.

The specialists on the faculty then would be readily available to laboratory personnel for consultation and laboratory specimens and materials could be used in the training of undergraduate and graduate students. A few States have such an arrangement, or some modificiation of it, but in most a much less satisfactory situation exists.

Up to this point we have been considering direct ways in which the veterinary college can cooperate in regulatory programs. There are also equally important indirect ways. One of these is by helping to overcome the regrettable attitude among veterinary students that regulatory work is a third-rate outlet for their professional talents--that it is something you settle for as a last resort if you have no money to build a veterinary hospital.

Students must be made to understand that regulatory work is a form of veterinary practice--an honorable, stimulating, and gratifying area of practice. This we can do by teaching students more of the romance of animal disease control. There are few more inspiring stories than those of the conquest of animal diseases, particularly those of public health significance.

Government could assume a more active role here, too. Nearly all applicants to veterinary colleges state that they intend to enter private practice, yet fewer than two-thirds of them actually do. The implication seems clear: for most citizens, "doctoring" a sick animal is all there is to veterinary medicine.

Government veterinarians could help us acquaint our students with the virtually unknown attractions and importance of careers in animal disease control. How many people, even adults, realize that the disappearance of the once familiar human hunchback from the American scene is a tribute to the conquest of bovine tuberculosis by veterinarians? Government can help, too, by sending only their most enthusiastic (therefore most inspiring) regulatory veterinarians to the colleges to speak to students and explain regulatory programs to them.

I should not like to leave with you the impression that I think more is wrong than right between the colleges and the regulatory agencies. On the contrary, I believe that there has been increasing cooperation during the past several decades.

Here in Michigan we have an outstanding example of cordial working relations between Federal, State and college veterinary personnel. But it would be inaccurate to say that our situation is ideal or could not be improved. The important thing is that it is being improved and all concerned are in basic agreement on what is needed for continuing improvement. Primarily it is a matter of more and better communications.

VETERINARY ACCREDITATION STANDARDS

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There is an intimate relationship between brucellosis and tuberculosis with respect to the activities of accredited veterinarians and their participation in these cooperative programs. When we consider performance standards for accredited veterinarians, it is difficult to divorce this point entirely from basic qualifications needed to function properly in this capacity. Therefore, I would like to discuss briefly both aspects of the problem, with emphasis being given to standards of performance as we believe they should be carried out.

Accreditation of veterinarians has a relatively long history. The first need for establishing standards of performance for veterinarians cooperating in field projects developed in the early stages of the tuberculosis eradication program in 1917. It was only two years after that date, 1919 to be exact, that the first listing of so-called "approved" veterinarians was established. The approved veterinarian was one who had been authorized to conduct tuberculosis tests on cattle moved interstate. In other words, during the early phases of the tuberculosis eradication project, there was a keen realization that full confidence must be established in the testing conducted as part of the eradication campaign. This means that for about 40 years we have known something either identical or very much like our present accreditation standards.

Over that period of time, we have listed approximately 20,000 individuals who have been designated as either "approved" or "approved and accredited" veterinarians. Within recent years, the word "Approved" Veterinarian has been eliminated in preference to our present term of "Accredited" Veterinarian.

The reasons behind setting up the initial approved and later the accredited category were the same in 1919 as they are today. There is no question but that the performance of accredited veterinarians has materially improved over the period of time this classification has been in operation. However, we are still faced with certain rather serious problems with respect to the participation of accredited veterinarians in disease control and eradication programs. It is in connection with these deficiences that I would like to discuss some of the points brought out in our more recent study of these situations in connection with cooperative programs. To begin with, the accreditation qualifications were based originally on their having graduated from an approved veterinary school, together with receiving the endorsement of appropriate livestock sanitary officials in those areas where they were requesting accreditation. For the most part, these same provisions have prevailed throughout the years since accreditation was first established. For several years, it was also required that veterinarians pass an accreditation examination. However, these tests finally developed into such a

set pattern that their value from the standpoint of qualifying veterinarians for accreditation was largely lost. In fact, at one time it was finally agreed that anyone could pass an accrediting examination and that very little knowledge of disease control work was required. This situation continued up until 1948 when it was decided something should be done to improve the accrediting procedures. As a consequence, the examinations were strengthened so that the abilities of applicants were more fully revealed. As might be expected, vigorous objection to these examinations developed throughout the country after a significant number of graduating veterinarians failed to qualify for accreditation. It was most interesting to observe, however, that within the next two or three years a great change occurred in the ability of applicants to answer correctly most of the difficult questions connected with this examination. There was no question but what this more rigid examination procedure accomplished a great deal in stimulating increased interest in the profession for regulatory veterinary medicine. After a period of years in which the credit levels remained constantly high on the accreditation examination, it was considered advisable to discontinue these tests. From this point on, an effort was made to work with the veterinary schools themselves in order to develop more emphasis on regulatory veterinary medicine. This program was handled through the Committee on Veterinary Education established in the Agricultural Research Service. The committee has continued to function in an effective manner and has been able to work constructively with all veterinary schools in the country in establishing courses designed to provide better instruction along lines suited for qualifying students as accredited veterinarians.

I was particularly pleased to hear Dean Armistead discuss plans here at Michigan State University which would provide for effective training of veterinary students along these lines. I am sure there is a growing sense of responsibility on the part of most veterinary schools at the present time to provide improved instruction in the field of regulatory veterinary medicine.

In 1957 following a series of conferences with the deans of the veterinary schools, it was decided to reinstitute some preliminary examinations as a means of orienting the students to current trends in regulatory veterinary medicine. There is reason to believe that the type of examinations being provided at the present time, together with current information available on the subject, will be helpful in developing more interest and higher qualifications of veterinary graduates applying for accreditation in the future. The primary purpose of these new examinations is to bring to the attention of graduating veterinarians newer developments in the field of regulatory veterinary medicine. For the most part, these preliminary examinations have shown that veterinary students are reading the literature provided in this connection. The grades are standing up very well. It still remains to be seen whether or not these examinations will be continued in the future, but, in any event, whether they are discontinued or not there is reason

to believe they have been doing a worthwhile job in focusing attention on the responsibilities of the accredited veterinarian in line with present day standards. Insofar as the Department of Agriculture is concerned, it has a number of definite responsibilities with regard to the activities of accredited veterinarians. One example is the control of export and interstate movements of animals. Unless such movements are effectively controlled, the progress already made in our disease control and eradication programs can be seriously jeopardized. There is also the important responsibility of detecting and suppressing outbreaks of diseases before they become a hazard to the livestock industry throughout the country. The Department is likewise concerned about its responsibility in cooperating with the various States on all State-Federal disease control and eradication programs.

In general, we have more or less taken for granted that the accredited veterinarian is fully aware of his responsibilities in all fields of regulatory medicine. Perhaps we have been negligent in this respect by not determining the qualifications of all accredited veterinarians and failing to provide current information on new developments in this specialized field. It is to be emphasized, of course, that for the most part the accredited veterinarian is conscientious and anxious to do the best job possible. A good job is not always possible, especially when the full scope and responsibilities of these activities are not fully understood.

Until such time as definite performance standards have been established, we will be faced with the necessity of having to operate with accredited veterinarians not fully competent to carry out their responsibilities. At the present time, consideration is being given to developing guide lines that will be helpful in establishing a basic pattern for the field performance of accredited veterinarians. There are a few important points that need to be emphasized in this regard. One relates to the veterinarian issuing certificates for livestock and poultry inspections. Under no circumstances should these certificates be issued by someone other than the person actually making the inspections. There have been occasions when this was done and as a consequence the validity of the certificates involved was open to serious criticism. There are also occasions when properly prepared certificates are not submitted promptly to the appropriate officials. This inevitably results in great confusion and loss of confidence on the part of the industry in the certification procedure. We are also greatly concerned about the efficiency of testing conducted in connection with the tuberculosis eradication program. With the incidence of this disease now at a relatively low level, the accuracy of test procedures and interpretations must be higher than ever before. It is rather unfortunate that at this particular stage of progress in tuberculosis eradication we find ourselves with fewer experienced veterinarians available for testing than we had during the height of the campaign. It is important, therefore, that adequate training be given wherever necessary to insure that injections are properly made and interpretations of reactions are in line with recommended procedures.

With respect to cooperative disease control programs, it is essential that the accredited veterinarian be thoroughly acquainted with the program in which he is participating. He needs to be in a position to explain fully all aspects of the program to owners in order that full cooperation can be obtained from everyone concerned. In many cases, the veterinarian is in a position to advise the owner about precautions that should be taken to protect his herd against further exposure. Without proper advice along these lines, it is entirely possible that infection may be perpetuated or reintroduced into clean herds, therefore prolonging the time that successful completion of the program can be achieved.

It is extremely important in the case of tuberculosis and brucellosis that appropriate retests be conducted at designated intervals following the removal of reactors. In too many instances such retests are unduly delayed with resulting doubts being established in the mind of the owner who has been advised of the need for prompt removal of reacting animals and retesting of his herd. It is essential, therefore, that the accredited veterinarian be alert at all times to the need for retesting infected herds and not ignore his responsibilities in this regard. Certainly, we are undoing a great deal of the benefits of testing programs if we simply remove the reactors and pay no attention to retests or cleaning and disinfection of premises after infected animals are eliminated.

Finally, it is important that the accredited veterinarian be alert to all reportable diseases. This includes the new and exotic types of diseases as well as those which have been more or less prevalent in this country for a number of years. The accredited veterinarian has the responsibility of reporting these diseases promptly to local livestock sanitary officials within the State. He must be able to recognize these new infections early enough to provide an opportunity to limit their extension. We have all seen the ravages that occurred in Mexico and Canada from foot and mouth disease. These are the situations we need to avoid through constant vigilance on the part of all veterinarians.

In conclusion, it should be pointed out that the vast majority of accredited veterinarians have contributed effectively to the conduct of nationwide disease control and eradication projects. Had it not been for their support, these programs could not have been advanced to the stages they have reached today. The accredited veterinarian is the man on the firing line and his performance can either make or break any effort to combat livestock diseases. To the livestock owner, he represents all agencies involved with projects of this nature. It will only be through the active support of the veterinary profession in general and the accredited veterinarian in particular that we can expect success in our efforts to eradicate such diseases as tuberculosis and brucellosis from our livestock populations.

THE BACTERIOLOGY OF TUBERCULOSIS

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The bacterium that is now known as Mycobacterium tuberculosis, or the tubercle bacillus, was discovered by the great German physician and bacteriologist, Robert Koch. His discovery, announced to the Physiological Society of Berlin in the spring of 1882, was quickly confirmed by others thus ending an age-old controversy about the essential nature of this disease. Some before Koch had supplied good evidence of its infective character but there were others, notably the great German pathologist, Rudolph Virchow, a contemporary of Koch, who believed the disease to be a granulomatous tumor with an hereditary basis.

The organism of tuberculosis was first seen by Koch quite accidently in film preparations of pus which had been stained with methylene blue and counterstained with Bismarck brown. The counter-stain acted as a decolorizing agent for other bacteria and tissue elements; these lost their blue color and became brown. The tubercle bacilli, however, refused to yield their original blue color and thus were easily seen by virtue of their contrasting hue.

Almost immediately, Ehrlich, working in Koch's Laboratory, discovered a better staining method for demonstrating tubercle bacilli in tissues. Using aniline-gentian violet or aniline-fuchsin, the tubercle bacilli were more strongly and more distinctly stained than with methylene blue; however, since Bismarck brown would not remove these dyes from other bacteria and tissue cells, another decolorizing agent had to be found.

It was quickly learned that strong mineral acids (sulfuric or hydrochloric) would serve admirably; these bleached everything in the films except the tubercle bacilli. Since these organisms held fast to the dyes with which they were stained in the presence of strong acids, the term "acid-fast" was applied to them.

Ehrlich found that phenol solutions could be substituted for the aniline-water as the mordant for the staining solutions but he regarded the latter as preferable. Ziehl, and then Neelsen, working in contemporary German laboratories, preferred the carbol-fuchsin stain and this combination became more popular than the aniline-water mixture. The carbol-fuchsin stain soon became the standard method used in most laboratories. It is the standard method of the present time.

Original staining with carbol-fuchsin followed by decolorization with mineral acid and counter-staining with methylene blue is now known as the Ziehl-Neelsen method of staining tubercle bacilli, although Ehrlich really deserves the credit for developing the method.

THE PROPERTY OF ACID-FASTNESS: First discovered in the tubercle bacillus, the property of acid-fastness has been found in later years in a fairly large group of bacteria and in some of the higher fungi. The organism of leprosy (Hansen's bacillus), the organism of Johne's disease, the causative organism of a number of infections in cold-blooded animals, and the organism of rat leprosy are all acid-fast. So are a large group of organisms found commonly in the soil and elsewhere and which are regarded as purely saprophytic forms.

The property of acid-fastness, therefore, is not diagnostic for tubercle bacilli. The property is very useful for finding these organisms in tissues and exudates, however, and when they are typical in size, shape, and grouping, when they are derived from lesions which have the typical appearance of those of tuberculosis, and when they occur in the discharges from organs in which there are lesions consistent with those usually found in tuberculosis, routine diagnoses are commonly and reasonably accurately made on the basis of the acid-fast stain. For research and critical purposes, however, criteria in addition to acid-fastness must be used to identify tubercle bacilli.

The property of acid-fastness is associated with a high lipid and wax content of the bacterial cells. All of the acid-fast bacteria take up aqueous dyes more reluctantly than other bacteria. It is necessary to allow the staining solution to act for a long-time period, or to hasten the staining action by heating the dye solutions. Once the dye has penetrated the acid-fast cell, it is given up just as reluctantly. Only long-continued action of the acid solution will bleach it.

PATHOGENICITY OF TUBERCLE BACILLI: In his second and more complete paper on "The Etiology of Tuberculosis," published in 1884, Koch recorded studies on 98 human and 34 animal cases of the disease. The characteristic bacillus was identified in all of these. Forty-three pure cultures of the organism were obtained and studied. The disease was induced by inoculation in nearly 500 animals, mostly guinea pigs and rabbits. The infectious nature of the disease and the characteristics of the causative organism were so thoroughly clarified and described that today, 85 years later, our knowledge of these matters has not been greatly expanded; only a few inaccuracies have been corrected and a few lacunae in our knowledge have been filled.

The most important error that has been corrected was Koch's original belief in the unity of the agent of tuberculosis in all host species. It was not until 1890 that Koch changed his views by admitting that the agent of avian tuberculosis was not identical with that of mammals, and not until 1901 that he conceded the organism of bovine tuberculosis was not identical with that found most commonly in man.

Theobald Smith, in this country, supplied convincing evidence as early as 1896 that there were differences in cultural features and

pathogenicity between the human and bovine types, but so strongly did Koch's views dominate the scientific world at that time that little attention was paid to Smith's papers.

Koch and most of the rest of the medical world held the view during the latter part of the 19th century that while most cases of human tuberculosis were contracted from other people, nevertheless a vast reservoir of human tubercle infection existed in animals, especially cattle.

In 1901, at the British Congress of Tuberculosis, Koch created a sensation by announcing his change of view. He reported that he had found, by experimentation, that bacilli which had been derived from human lesions had very little pathogenicity for cattle.

He also reasoned, but without experimental evidence in this case, that bovine-type tubercle bacilli probably had little pathogenicity for man, and played little or no role in the epidemiology of the human disease. In general, these views have proved to be correct although we know, of course, that bovine-type organisms are more important in human pathology than Koch thought.

TYPES OF TUBERCLE BACILLI: Four types of tubercle bacilli are recognized in the latest edition of Bergey's manual, the bacteriologist's bible. One of these is *Mycobacterium microti*, or the vole bacillus. This organism produces a progressive tuberculosis-like disease in voles and other species of rodents. It appears to be nearly completely innocuous for man and the domesticated animals. It has little interest for us except for the fact that Wells and his colleagues in England attempted, with some success, to use the organism as a vaccine for human and bovine tuberculosis. We will not consider this organism further.

The three types which concern us are commonly known as the human, the bovine, and the avian. Bergey names these *Mycobacterium tuberculosis*, *Mycobacterium bovis*, and *Mycobacterium avium*, respectively. The differences between the human and the bovine types are largely quantitative rather than qualitative, hence I think many will disagree with Bergey and continue to regard these as distinct types of a single species rather than different species. A considerable gulf exists between the mammalian types and the avian type--in cultural features, in pathogenicity, and in immunogenicity--so there can be no serious quarrel with those who wish to regard the latter as a different species.

There is little point here in considering the details by which a trained laboratorian can identify tubercle bacilli and differentiate between the several types. A combination of cultural features and pathogenicity for several laboratory animals is the usual basis. The avian type infection may be distinguished from the mammalian types by allergic and serologic means, but these methods will not serve to distinguish between infections of human and bovine-type bacilli.

The usual criteria for identification will generally identify unknown organisms in one of the three classical types, but occasionally strains are found that are atypical, i.e., they do not fall clearly into any one of the standard types but have intermediate characteristics. The difficulty most frequently encountered is in differentiating organisms as human or bovine. Often when such strains are inoculated serially into animals their aberrant character is lost and typical characteristics appear, but sometimes this fails and a clear classification is not possible.

Some of the early workers thought that the human organism might be changed until it acquired the characteristics of the bovine by inoculating it serially in cattle, but this has not proved to be possible. Some degree of original pathogenicity may be lost by passing tubercle bacilli through abnormal hosts, yet they cling to their original characteristics. In other words, it has not been possible to force variation to such a degree that the characteristics of the strain change from human to bovine, or from bovine to human.

RESISTANCE OF TUBERCLE BACILLI: Since tubercle bacilli do not produce spores, they are not materially different in their reactions to heat and chemicals than other bacteria. Ordinary pasteurization temperatures destroy them; in fact it was the presence of tubercle bacilli in much of our milk a half century ago, more than anything else, that induced health authorities to require its pasteurization.

To chemical disinfection, especially acids and alkalies, tubercle bacilli are somewhat more resistant than many other bacteria. They are readily destroyed by many of the phenols, cresols, and cresylic acid compounds which are included in the Department of Agriculture's list of approved disinfectants. Preliminary application of hot alkali solutions in practical disinfection of premises has for its purpose not the destruction of tubercle bacilli but the removal of organic materials in which the bacilli are embedded, thus making them vulnerable to the disinfectant which follows.

Tubercle bacilli exhibit no greater resistance to drying than other bacteria. When exposed to air in thin films on slides protected from direct sunlight, they usually lose viability within a few hours. Exposed to direct sunlight, the bacilli in such films usually succumb within a few minutes.

As in the case of most other bacteria, tubercle bacilli are not harmed by low temperatures. Freezing temperatures and even deep-freeze temperatures serve to preserve rather than destroy them. In putrefying animal tissues, tubercle bacilli preserve their characteristic morphology and staining reactions long after all other recognizable elements have disintegrated, and there is evidence that they retain their viability rather well under such circumstances.

There is experimental evidence indicating that mammalian tubercle bacilli may retain viability and virulence in moist soil for well over a year, and avian type organisms apparently are even more resistant under these conditions. Schalk and his fellow workers in North Dakota succeeded in demonstrating virulent organisms in carcasses of birds that had been deeply buried in the soil for more than two years.

These workers isolated avian-type bacilli, fully virulent, from the soil of heavily contaminated poultry yards which had contained no birds for nearly four years. It is obvious from these observations that tubercle bacilli have remarkable stamina in the environment providing they are protected from direct sunlight and loss of moisture.

These observations indicate that in endeavoring to free premises from tubercle infection, the removal of infected animals alone is not enough. The elimination of infected animals will serve to dry up the source of tubercle bacilli since they do not multiply outside of affected animals but the residual contamination of the environment must be considered.

The removal of accumulated debris, the scraping and removal of the top soil layers in muddy barnyards, the filling of mudholes and the draining or fencing off of wet spots in pastures, are all means of reducing the hazard of leaving infection to carry on the disease in clean replacement cattle.

The cleaning and chemical disinfection of watering cups, water troughs, mangers, floors, stanchions, barn walls, and other objects that may have been contaminated by contact with diseased stock is an essential part of the procedure of removing as much residual infection from premises as possible.

Alkaline solutions, applied by a power spray while hot and followed by soaking with the disinfecting solution, is required for this. Even more effective are sprays containing disinfectants incorporated with whitewash since such solutions not only exert the necessary bactericidal action but also supply a protective germicidal coating.

How often reinfection of herds occurs as a result of persisting soil infection, I do not know. Several authorities have expressed doubt that it occurs often, if ever. It is a point that is practically impossible to prove, one way or the other. I should expect that it must occur occasionally. The fact that we have eliminated tuberculosis from thousands of herds by using a limited number of tuberculin tests, slaughtering the reactors, and cleaning and disinfecting the premises with little or no attention to pastures, indicates that soil contamination cannot be a very important factor in perpetuating the disease. In the avian disease, the situation is quite different, since it is quite clear that soil contamination does play an important role in this disease.

TRANSMISSION OF TUBERCLE INFECTION AMONG ANIMALS: By experimental inoculation of tubercle bacilli into susceptible animals it can easily be demonstrated that tuberculosis begins always as a localized disease. If the virulence of the organism is not too high and the amount of the inoculum is not excessive, the disease may continue as a localized process, healing may occur, and the animal may recover without showing any signs of systemic disease.

If the animal species is highly susceptible, if the virulence of the organism is high, and if the dose is relatively large, the local lesions may quickly yield bacilli to the lymph channels draining the area of the initial lesion and secondary localizations will result. Sooner or later the disease is apt to spread by this sort of extension through the lymph channels until eventually blood infection occurs and the disease then becomes generalized.

The blood stream may be reached by way of the thoracic duct but doubtless there may be short-cuts at times by ulceration of the tuberculous process through small veins. Multiple lung lesions usually are the first result of generalization since the capillary bed of the lungs is reached first. Furthermore the lung tissue of mammals appears to have a special susceptibility to tubercle formation.

In the natural disease, infections occur most commonly as a result of inhaling or ingesting bacilli. In birds, swine, and young calves the lesions of tuberculosis are found most commonly in the intestinal wall, in the mesenteric lymph nodes (in mammals), and in the liver and spleen. Lung lesions are seldom found in birds but they are frequent in swine and calves, but obviously of secondary occurrence.

These facts point toward infection by ingestion. These species are infected, as a matter of fact, by swallowing infected fecal material from the surface of the ground, or by drinking infected milk.

In man and cattle, on the other hand, the disease is most often localized in the lymph nodes of the head, in the nodes draining the lungs, or in the lungs themselves. These localizations suggest infection by inhalation of infected droplets, and other evidence supports this hypothesis.

Experimental feeding of adult cattle with tubercle bacilli has, in some instances, produced lung lesions without evidence of disease in the intestines or mesenteric lymph nodes. The intestinal tract of cattle seems to possess a moderate degree of resistance to tubercle infection, according to Ravenel, Griffith, and others, hence when moderate doses of the organism are encountered the gut apparently sometimes allows the infection to pass into the thoracic duct and eventually into the lungs without exhibiting lesions at the port of entry.

Also, the finding of head lesions alone, a common finding in early tuberculosis in cattle, suggests that bacilli taken into the mouth or the upper air passages may reach local tissues by penetrating the mucous membranes of these regions, possibly through the tonsils. The extension of the disease from the nodes of the head to the thoracic organs through the lymph channels would be expected because of the anatomical relationships.

It has often been observed that tuberculosis spreads from cow to cow down the stanchion line. This has generally been interpreted as meaning that the disease is transmitted through infected droplets expelled by the coughing victim of the disease. Certainly this is an indication that the disease spreads best when animals live in close proximity to each other, but under such conditions infection by ingestion would also be favored through the use of common drinking cups and feed troughs.

It should be realized that tuberculosis is essentially a disease of domestication. It seldom occurs in wild animals living a free, out-of-door life but it is very common when these same animals are confined in small indoor quarters which often are not well tended. The disease is seldom a problem of range cattle, and usually when the disease occurs it is as a result of contact of range animals with dairy stock.

In man the disease did not become the great killer, "the great white plague," until the beginning of the industrial revolution when people, for the first time, began to congregate in great cities and to live in crowded dwellings. The disease flourishes only when individuals live inside of buildings in intimate contact with each other. It is then that the tubercle bacillus finds its greatest opportunity to pass from host to host, and whether this occurs through the air passages or the mouth is pretty much of an academic question.

IMMUNITY TO TUBERCULOSIS - NATURAL AND ARTIFICIAL: Much work has been done and much has been written on the subject of immunity to tubercle infection in man and animals. Soon after the discovery of the causative agent, search for an effective vaccine to prevent or favorably affect the course of the disease in man and animals was undertaken. Many different kinds of vaccines have been made, tried, and advocated for a time only to have them discarded later when it became evident that initial enthusiasms about their value had been grossly inflated. Up to the present time, it can safely be stated, no very adequate vaccines for tuberculosis have been discovered or developed.

Heat and chemically killed bacterial vaccines, and extracts of tubercle bacilli have been used by many in attempting to heighten resistance to the disease but to no avail. Several have tried to use acid-fast bacilli, other than tubercle bacilli, as vaccines against the disease but these have failed.

There is evidence, however, that living, attenuated cultures of tubercle baccilli are able to induce a useful grade of immunity, and such vaccines have been used on a large scale in the past. The bovovaccine of von Behring, which had a considerable vogue for a few years, really gave impressive evidence of efficacy in reducing the ravages of the disease in cattle but when it was learned that the vaccine consisted of virulent human-type tubercle organisms and that many vaccinated cattle shed these organisms in their milk, enthusiasm for the vaccine died out.

Of the myriads of anti-tuberculosis vaccines that have existed in the past, I am aware of only one that has any vogue today. This is the BCG vaccine (Bacillus of Calmette and Guerin). This vaccine consists of a strain of the bovine type which was cultivated for many years by the French workers on a culture medium saturated with ox-bile. The bile served as an attenuating agent, the original virulence being gradually lost as cultivation in its presence continued. When it had reached a nearly avirulent state, it was used as a vaccine.

In surroundings where the disease is frequent and dangerous exposures unavoidable, BCG is administered to young animals and human infants before they have been exposed to the natural disease. This vaccine has now been used for more than 30 years and millions of human infants have received it.

Many of the early workers thought the vaccine was unsafe, and an accident in Lubeck, Germany, in which 75 human infants died from what was considered to be inoculation tuberculosis following BCG vaccination greatly increased the apprehension about its safety. Time has shown, however, that the properly-made vaccine is safe when used on tuberculin-negative individuals.

There are some workers who still argue that the statistical data, upon which the good results attributed to the vaccine are based, are faulty and they doubt its value. The majority of workers feel, however, that the vaccine has value in man. In the United States the vaccine is not used on a large scale but it is advocated and used on many tuberculin-negative people in special hazard groups, such as young physicians, medical students, nurses, attendants in sanitoria, etc.

There seems to be no value in general application here since the incidence of tuberculosis in man has decreased to a relatively low level. In some other parts of the world where the disease is still common, BCG vaccine is used extensively on human infants. In some of the Scandinavian countries physicians are required by law to administer it to all new-born babies.

BCG vaccine was used by its original sponsors on cattle with good results being reported. Later studies by others have yielded equivocal results. So far as I am aware this vaccine is not being used on cattle in any part of the world today.

Calmette and Guerin claimed that their vaccine achieved what they called a state of premunition. This term indicates a special form of immunization, one in which the state is created by a pre-existing, low-grade infection. The low-grade infection protects against a super-infection by a more virulent strain. To accomplish premunition it is necessary that the living vaccine be administered some time before exposure to the virulent disease occurs. Accordingly human infants are given the vaccine on the first or second day of their lives and held in isolation for about three weeks before being released to live in their infected environments. The same technic is used, of course, on animals.

BCG and other living vaccines made from tubercle bacilli will cause the treated individuals to become allergically sensitized. Such animals will react to tuberculin, hence vaccination of cattle and other domesticated animals in this country has not been done, except on an experimental basis, and it should not be done since it would seriously interfere with the procedures we are using to reduce the disease to its present low incidence and which we shall have to continue to use to complete the eradication task. If cattle vaccination with BCG has any value it will be only in areas of the world where the incidence of the disease is high and where other methods of reducing it are not feasible.

If there is any difference in the degree of resistance to tuberculosis of individuals within a species, it is not very great. It has long been recognized, however, that the tissues of individuals harboring local infections react differently to a new infection superimposed on the first than those of other individuals who are encountering the infection for the first time.

When small numbers of virulent bacilli invade the body for the first time, a mild tissue reaction occurs around the clump of multiplying bacteria. Ordinarily this takes the form of proliferation of monocytic cells which become known as epithelioid cells, and the area is invaded by small numbers of lymphocytes. The granulocytes ordinarily are conspicuous because of their absence.

As the lesion grows in size necrosis generally appears in its center and ordinary connective tissue cell proliferation forms a dense capsule around the whole structure. This is a primary tubercle. There is no acute inflammation in a primary tubercle.

Frequently the organism becomes completely walled in by the proliferating local cells which compress and obliterate the small blood and lymph vessels which were in the site before the tubercle formation began. Since the clump of organisms is in an avascular location and they are unable to escape in many cases, the bacterial invasion of the body is brought to a halt.

In man, and occasionally in animals, such lesions are detected during life by the use of radiology. The individual feels well; he was wholly unaware that such lesions existed before they were demonstrated by the X-ray machine. He harbors an "arrested" or "healed" lesion. He is a tubercle-infected person but he is not suffering from active tuberculosis. Such persons may live out their normal life spans without showing any clinical signs of disease.

Fifty years ago, more than 95 percent of all mature persons living in the great cities of Europe and America harbored such lesions. Their scarcity today in this country attests to the great progress which has been made in controlling tuberculosis since 1900.

Localized healed lesions of tuberculosis also occur in cattle and other animals, though perhaps not so frequently as in man. Their histological structure in the early stages is the same as of those found in man. In the later stages, calcification occurs in all species, but in cattle it probably is a little more pronounced than in man.

After a primary tubercle has been in existence for a short time, a state of allergic sensitivity is developed by the host animal. This may account for the encapsulation and frequent isolation of the primary focus from other parts of the body. When new bacilli enter the body from the outside, or when bacilli escape from the primary lesions, a very different type of reaction develops at the points where the new localizations occur. Acute inflammatory reactions now occur around the new foci of infection, exudates accumulate, the lesions tend to spread, and early necrosis occurs. Koch probably was the first to observe this altered reaction. His observations have become known as the Koch phenomenon.

A series of guinea pigs which previously had been infected with bacilli of low virulence, and another series which had had no previous contact with tubercle bacilli were inoculated simultaneously into the leg muscles with a virulent strain. The previously infected animals reacted to the new inocula very promptly with fever and prostration, acute swelling at the inoculation site followed by local necrosis of tissue, ulceration, and discharge of the content of the abscesses. The local lesions then healed and the animals became well.

The previously uninoculated animals, on the other hand, showed slowly developing lesions near the point of inoculation, followed by generalization, rapid emaciation, and death from tuberculosis at a time when the first group were still in relatively good health.

Calmette and Guerin made observations on cattle with similar results. Using a group of calves, part of which were tuberculin reactors and part negative, they injected virulent tubercle bacilli intravenously into all. The tuberculin-reacting animals (already infected) were made acutely ill by the injection but all recovered in a short time and they then continued

as if nothing had happened. The non-reactors, however, showed a little immediate reaction to the virulent inoculation but they gradually developed symptoms of acute tuberculosis.

There has been much controversy in the literature about whether allergy and immunity are the same or wholly unrelated phenomena. Rich and others in recent years have produced data indicating that they are not identical. Nevertheless it cannot be denied that generally neither is found without the other. If they are not identical then they must be closely related.

Krause long ago pointed this out and called attention to the fact that allergy in tuberculosis seemed to stand alone among all immunological reactions in relation to enhanced resistance of the host; that whereas all of the usual antibodies could be induced in animals with dead bacilli or extracts of tubercle bacilli, these were not accompanied by enhanced resistance, neither were they capable of establishing a state of allergy; that both resistance and allergy were produced only by living organisms capable of multiplying in tissues and stimulating the formation of tubercles.

It must be said that it has been demonstrated that dead organisms can stimulate a state of allergy but the condition is fleeting. Also there is evidence that dead organisms will produce some resistance to infection, which also is fleeting. The parallelism between allergy and enhanced resistance is very striking, but it is not for me to argue with those who have spent their lives working with tuberculosis on the relationship, or lack of relationship, between the state of allergy and the immune state.

The view of Allen Krause which prevailed for many years and is still accepted by good bacteriologists in spite of recent challenges was that hypersusceptibility is actually a protective device in that it enables the host to react quickly and effectively to wall off and confine bacilli that find their way into tissues.

He considered that the real threat of tubercle bacilli to their host lay in the fact that their waxy coating prevented rapid dissolution of their cells, which in turn prevented release of their toxic substances and therefore they did not stimulate, rapidly enough, the usual defensive mechanisms of the body. This allowed too much extension of the disease throughout the body before the defensive mechanisms of the host had been effectively aroused.

The degree of protection provided by premunition with cultures of little or no virulence, or by the natural disease, is always limited in its effectiveness. Certainly it does not prevent infection and it does not always prevent progression of the disease to a fatal conclusion.

MECHANISM OF THE TUBERCULIN REACTION: Tuberculin was discovered by Koch in 1890 and was, at first, advocated as a curative agent. Myriads of different types of tuberculin have been used in the past. Many have had special virtues claimed for them but most of these have been found baseless. All tuberculins, whether made from filtrates of cultures or extracts of tubercle bacilli are essentially alike in that they contain water-soluble tuberculo-protein derivatives.

The first tuberculins used extensively in veterinary medicine were produced by growing tubercle bacilli in glycerin broth until maximum development had occurred, then killing the organisms by prolonged boiling of the culture, and finally filtering out the dead organisms with Berkefeld or other filters. It was a clear golden fluid with an almond-like odor. For some uses it was concentrated by evaporation. Preservation usually was obtained by the addition of a small amount of phenol.

In more recent years tuberculin has been produced in essentially the same way, except that the culture fluid is a synthetic mixture of chemicals which contains no proteins. Not only does better growth of the organisms occur on this medium but the absence of commercial peptone and meat extracts, which were in the old broths, provides a product much less contaminated with extraneous substances.

The official tuberculin prepared in this country for use on cattle has always been made from human-type strains. For use on man, usually a purified tuberculin known as P.P.D. is used. This purified protein derivative is made by chemically extracting the active fraction from tuberculin prepared on a synthetic fluid medium. This product has been used on cattle experimentally in this country. In the British Isles it is the standard product used. Limited experience seems to indicate that the purified product has few advantages in cattle over the crude filtrates.

The tuberculin reaction is generally regarded as an example of an allergic reaction. As a result of the growth of tubercle bacilli in the body and the stimulation of a cellular response, all of the body tissues become hypersusceptible to tuberculo-protein. Whether this is then introduced with living, or heat-killed organisms, or in the form of extracts of such organisms, an acute inflammatory response results at the point of injection. This is known as the <u>local</u> reaction.

If larger quantities are introduced so that appreciable amounts of tuberculin reach the general circulation, the tuberculous tissues, wherever they may be, show signs of acute inflammation. This has been called the <u>focal</u> reaction.

Focal reactions are accompanied by secondary general changes such as fever, chills, malaise, and mental depression. This is called the <u>general</u> reaction.

As diagnostic procedures, the intradermal and ophthalmic tests are examples of local reactions; the subcutaneous or thermal test depends upon the stimulation of the diseased foci and the development of a general reaction. Since there is evidence that tuberculous lesions may be stimulated into greater activity by doses of tuberculin great enough to elicit the general reaction, the thermal test is not used on man.

Since this is not an objection in animals inasmuch as reactors generally are destroyed as soon as they are identified, the test is still a useful one, not so commonly used today as formerly because it is a more laborious and time-consuming one than the intradermal method. The latter is practically the only one now used on man, and the one generally employed on animals. On the whole it probably is the most sensitive test we have, although some animals that fail to react intradermally will react thermally. Many more that fail to give clear-cut reactions to the thermal test will react typically to the intradermal method.

The lesson of this experience is that it is well, in important cases, to use both methods. If this is done it is best to apply the intradermal test first, since much less tuberculin is used than in the thermal test and therefore desensitization is much less apt to occur.

Although the tuberculin test is highly specific and as reliable as any biological test that we have, it is not infallible. Tuberculin made from human-type bacilli is as good in every respect for detecting bovine tuberculosis as that made from bovine-type organisms, and vice-versa. This is one of the several indications of the closeness of the relationship between these two types.

For testing for infections believed to have been caused by avian-type bacilli, mammalian tuberculin will not serve; it is necessary to use tuberculin made from avian-type organisms. This is one of the indications of the diverseness of mammalian and avian-type organisms. Occasionally, however, animals affected with avian-type organisms will apparently react to mammalian tuberculin, and vice-versa.

It is well-known too, that animals affected with Johne's disease usually will react to avian tuberculin, and birds affected with tuberculosis usually will react to Johnin. These are indications of lack of specificity, or, to put it another way, the possession by these organisms of some common or group antigens.

When tuberculosis of cattle was common in many parts of this country 30 years ago, occasional aberrations in the tuberculin test results did not cause very much concern, although they were recognized. These aberrations are of much greater concern today since tuberculosis has been reduced to a low incidence.

Many years ago I stated that if we continued to place sole reliance on the tuberculin test for diagnosing bovine tuberculosis, we would be

finding some reactors and slaughtering uninfected animals long after the disease had been eradicated. I repeat this assertion now. Also, and this aspect of the situation is even more serious, the tuberculin test misses some cases of tuberculosis.

It has long been known that advanced cases of the disease were so saturated with tuberculo-protein derived from their own lesions that they became insensitive to doses of additional tuberculin injected for diagnostic purposes. Why less advanced cases are so frequently missed is a matter for speculation. In many cases it is probable that the failure is not so much the fault of the animal as it is of the observer who makes the test.

It is obvious, I think, that we need new approaches to the diagnostic problem in bovine tuberculosis. During the last 10 years, according to statistics provided by the Department of Agriculture, the incidence of bovine tuberculosis has not been reduced. I raise the question as to whether we can accomplish much more than we have with our present methods.

Can we afford to continue to test and retest all of our cattle indefinitely? Can we hope for eventual eradication, using present methods? Frankly, I doubt it. I think that new methods and approaches will have to be found. The more complete tracing of slaughter-house cases has been extremely helpful. This approach to the finding of cases should be developed as fully as possible. Even now it is the means of finding more infected herds than the tuberculin test.

DIAGNOSIS OF TUBERCULOSIS BY SEROLOGICAL MEANS: Various workers have demonstrated precipitins, agglutinins, and complement-fixing antibodies in cases of tuberculosis hence, theoretically, tests for these antibodies could be used for the diagnosis of the disease. In practical work, however, none of these tests have served a very useful purpose.

The agglutination test is difficult or impossible in mammalian tuberculosis because the causative organisms occur naturally in the rough or spontaneously agglutinable form. Some success has been achieved in avian tuberculosis, however, and the agglutination test may possibly be developed into a practically useful procedure. Dubos and Middlebrook, a few years ago, developed an hemagglutination tests for tuberculosis using sensitized sheep cells for antigen. This test has some possibilities.

The most useful of the serological tests for tuberculosis is the complement-fixation procedure. More or less success has been achieved by many workers with a great variety of modifications of this method. There is no doubt that most cases of tuberculosis in man and animals will react to these tests but there are too many non-specific reactions to make it practically useful.

In man it is stated that these false reactions approximate 10 percent, and I should judge from the experience which Zeissig and I had

with the test in Johne's disease that the percentage of false positives is at least as large. There are differences of opinion as to whether these false reactions are due to sensitizations with other acid-fast bacilli, or to other unknown factors.

Cattle suffer infections with Johne's disease and with cutaneous lesions in which acid-fast organisms are demonstrable. Also the content of the alimentary canal practically always contains acid-fast organisms which are presumed to be of soil origin.

We know that animals suffering from Johne's disease and the skin lesions will usually give positive reactions to the complement-fixation test when the antigen consists of tuberculo-proteins. We wonder if normal animals may be sensitized to this test, and perhaps to the tuberculin test as well, by organisms of the type that we see in the alimentary canal and which are believed to be wholly saprophytic chance contaminants of the forage. The hypothesis sounds attractive but there is little experimental evidence to support it.

CHEMOTHERAPY OF TUBERCULOSIS: Chemotherapy of tuberculosis has been attempted since shortly after the discovery of the causative organism. There were many claims of limited success with gold salts and other chemicals but most of these eventually were abandoned as worthless. At present, chemotherapy of tuberculosis is limited to the disease in man since it is neither wise nor practicable to attempt treatment of the disease in animals.

With the advent of the sulfa drugs it was found that some of them exhibited marked inhibition of tubercle bacilli *in vitro*, but the effect *in vivo* in experimental animals was much less encouraging. In 1942, a sulfone compound, known as promin, was introduced by Feldman, Hinshaw, and Moses. It gave very encouraging results in experimental tuberculosis of animals and upon the natural disease in man, but the compound had so much toxicity that it later was abandoned.

Streptomycin was shown to have a marked suppressive effect on tuberculosis in guinea pigs in 1944 by Feldman and Hinshaw and a little later this drug was used for the first time in treating human patients. I think it can be said that streptomycin was the first drug found to have marked efficacy in tuberculosis and at the same time to have a level of toxicity low enough to make it possible to use it in effective dosage. The tendency of tubercle bacilli to develop drug-fastness toward streptomycin is unfortunate so far as its future is concerned.

Para-aminosalicylic acid (PAS), and isoniazid have been introduced more recently and these, with streptomycin, are the most effective antituberculosis drugs that we have. None of the drugs should be regarded as effective cures of human tuberculosis; Old Mother Nature is still more important than anything that man has devised. They help in suppressing the tubercle bacilli, however, and this perhaps is all that we may ever expect from drugs.

THEORY AND PRINCIPLES OF CLEANING AND DISINFECTION

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Cleaning and disinfection had their inception with the discovery of the germ theory of disease transmission. Semmelweiss, Holmes and Lister all advocated cleaning and disinfection as a means of disease control. Yet here we are discussing the theory and principles of cleaning and disinfection, although we have had 80 years of experience in practice. Why? We still are not sure of methods, and even if we are satisfied with methods that have been developed, we don't practice them properly.

Perhaps we are content with procedures and germicidal agents. In Sternberg's text on Bacteriology published in 1895 a list of disinfectants are presented for the disinfection of typhoid fever patient stools. Vincent in 1895 proved most of them were unreliable. In Rosenau's Preventative Medicine and Public Health, 1956, the following list appears: Bleach, 3 percent; milk of lime 1 to 8; cresol, 1 percent; phenol, 5 percent; formaldehyde, 10 percent; unslaked lime, and hot water. Use two volumes to one of excreta, stir, allow to stand two hours.

Most are just as ineffective now as they were in 1895. Why do they appear in the latest texts on disease control? They are well publicized germicides and made acceptable by repeated publication in reputable texts.

If disinfectants can be poured in excess concentrations on soiled surfaces to destroy disease-producing microorganisms successfully, then there is no need to discuss theory and principles because no problem exists. Unfortunately, the disinfection practice has not changed in 62 years. The direct application of disinfectants to organic soil contaminated with disease-producing microorganisms does not necessarily result in surfaces free of disease hazard.

Although the properties of a good disinfectant generally include penetrability, the property of passing through organic soil to attack microorganisms is nil in most compounds. If a disinfectant does destroy microorganisms embedded in soil, it is not by penetration of the soil but by the property of deflocculation, the dispersing of soil into small particles, thus releasing the microorganisms from their protective layers of soil. The detergent-germicide functions in this manner very effectively provided the organic debris does not destroy the disinfectant.

The following data taken from the files of the author demonstrate that disinfectants have little or no penetration power.

Example 1. Two milking machines were carefully washed and sanitized. Subsequently after each use the machines were rinsed with cold water and stored for the next usage. Before each use, one machine was rinsed with

a hypochlorite solution and the other was rinsed with cold water. The following graph (Fig. 1) presents the daily bacterial counts of the milk for each machine for a period of 11 days.

After the fourth day, without washing except for a cold water rinse, the bacterial counts rose rapidly. Although the counts were somewhat lower on the chlorine rinsed machine, the bacterial increase was also rapid. This demonstrates vividly the inability of a chlorine sanitizer to cope with bacteria embedded in an organic matrix.

Example 2. An unpainted wall in a refrigerated area was badly contaminated. A prescribed area yielded 28,000,000 bacteria. A section of the wall, sprayed with 200 ppm. quaternary ammonium compound, yielded 11,000,000 bacteria. After washing with a tri sodium phosphate solution, the count was reduced to 380,000 and after rinsing, the same section yielded 53,000. After spraying with 200 ppm. quaternary ammonium solution, the count was reduced to 100 bacteria.

Here again the disinfectant was unable to cope with embedded bacteria. When the soil was removed, the exposed bacteria were readily destroyed and a surface relatively free of bacterial contamination resulted.

The writer could present many other examples but they would merely replicate the cases cited. The facts are that disinfectants lack penetrability, so soil must be removed from surfaces prior to disinfection. Disinfection must be predicated upon good cleaning. Another reason soil should be removed, is because of the dissipation of disinfectants caused by organic matter. Disinfectants are not specific for bacteria but attach to particles of organic matter. They are rendered ineffective either by adsorption on the surfaces of organic particles or by combining to form non-germicidal compounds.

In Figure 2 are presented the killing dilution of three disinfectants in the presence of varying amounts of serum. These data show that all three compounds are reduced in activity by the presence of organic matter, although those with high minimum killing dilutions are affected to a greater extent. All disinfectants are reduced in activity by the presence of organic matter. However, those with low phenol coefficients are less effected.

The presence of neutralizing agents on the surfaces to be disinfected also may affect the germicidal value of the disinfectant. For example quaternary ammonium compounds are neutralized by soaps and anionic wetting agents.

The pH of the surface to be disinfected also may affect the germicidal value of the disinfectant. A quaternary ammonium compound (1-1000) was checked at pH values of 5, 7 and 9. The results follow:

pH value of solution	Percent kill
5	55.6
7	99.2
9	100.

As you will note, the quaternary ammonium compounds become more germicidal in the presence of alkali.

On the other hand chlorine compounds become less germicidal. For example to produce 1 ppm. of germicidal chlorine at pH 4, only 1 ppm. of chlorine may be added to a solution, whereas at pH 10, 500 ppm. would have to be added to attain the same amount of germicidal activity.

Thus the surface to be rendered free of disease hazard must be prepared for disinfection by proper cleaning so that the disinfectant can be used effectively as a safety precaution to destroy all undesirable residual microorganisms.

What constitutes a clean surface? A clean surface is generally considered to be one that appears clean to sight and touch. This is a satisfactory measurement of cleanliness for areas not subject to disease organism contamination. In areas where disease hazard may exist, the area should not only be clean as measured by sight and touch but should also be free of undesirable microorganisms.

When a surface is cleaned mechanically most of the microbial population is removed with the soil. With proper cleaning, the residual bacterial population becomes negligible.

Example 1. In a study on milking sanitation, the machines were carefully cleaned with warm water, a good detergent and a brush. In the following table the results attained are compared to a comparable machine rinsed with cold water each day:

Days of testing	Rinse count of cleaned machine	Bacterial count of milk from cleaned machine	From machine rinsed with water
1	0	580	1,300
2	40	1,900	2,200
3	10	1,100	32,000
4	0	800	13,000
5	10	1,100	66,000

In this particular example there would be little need for treatment with a sanitizer because the bacterial population of the milking was insignificant. The low count does not necessarily mean that treatment with

a sanitizer should be omitted. It does demonstrate that the degree of contamination encountered after cleaning should be small. The sanitizer should always be applied as a safety precaution.

Example 2. A steam jenny was used for cleaning. A detergent was introduced so the steam acted as a propelling force for water and detergent. The steam was delivered to the hose line at a pressure of 90 to 120 psi. Micrococcus caseolyticus, an organism comparable to Mycobacterium tuberculosis in heat resistance, was introduced into the test soil to check the effectiveness of cleaning. The result of these tests follows:

Test Number	Initial No. of Organisms	No. of Organisms Surviving on Surface	Percent reduction on surface.
Comp. of 4 tests	623,000	Steam + detergent, 32,000	94.83
Comp. of 4 tests	82,000	Steam + detergent+ sanitizer 0	0

A high velocity stream of water and steam does an excellent job of soil removal. The addition of a detergent, of course, hastens the soil removal by increasing the speed of wetting the soil for easier removal. By adding a disinfectant, a residual layer of disinfectant laden water remains on the surface to destroy the remaining bacteria left after cleaning.

Water supplemented by vigorous brushing does a fair job of soil removal. However, for acceptable cleaning with a minimum of labor detergents should be used. The detergent makes possible the complete removal of fats, protein and carbohydrates.

Fats can be removed by either saponification or emulsification. Saponification occurs only in the presence of strong alkali and heat. Emulsification, the process of suspending fats and oils in water by breaking them into tiny droplets surrounded by the detergent, is produced by the action of soap and surface-active agents such as the sulphonated alcohols.

Proteins and carbohydrates are attacked by strong detergents such as caustic soda, tri sodium phosphate and sodium metasilicate. The process consists of breaking the substances into small particles, deflocculation, and suspending in the wash water.

With a strong caustic, caustic soda, there is also a dissolving action on the proteins. In strong alkali where the pH is above 12, germicidal action also occurs. It should be remembered that caustic soda or tri sodium phosphate, has little germicidal action on the tubercule bacillus. As a matter of fact, sputum specimens from tuberculous patients are treated with strong alkali to dissolve the mucous material, and to reduce the extraneous microbial populations prior to culturing for the tubercule bacillus.

Detergents also have the property of suspending power, i.e.-they increase the activity of the water to hold fine particles in suspension. A 0.3 percent solution of an alkaline detergent will hold approximately 1,000 ppm. of organic solids in suspension. If the organic solids are in excess of 1,000 ppm. then redeposition occurs. Suspending action is important because the soil should stay in the wash water until it has been flushed from the surface being cleaned.

Detergents should have wetting properties. The addition of soap or synthetic detergents to a detergent mixture reduces the surface tension of the cleaning solution. By using a wash water with reduced surface tension, the water penetrates the soil rapidly and thus speeds removal.

A discussion of ingredient content of detergents would be of little help because the worker will not prepare a detergent mixture. There are many good detergent formulations on the market. Every detergent manufacturer has a formulation designed for each specific job. Your local dealer can supply you with a desirable product cheaper than you could formulate your own product.

To obtain good cleaning of floors, walls and other surfaces, use a warm water containing approximately 0.5 percent detergent. Use ample amounts of wash water and allow sufficient contact to wet the soil. Apply mechanical action to the surface with a brush or a high velocity stream of water. Keep the wash water clean to assure maximum suspension of soil. Rinse with clean water to remove wash water and soil. If the cleaning has been properly done the cleaned surfaces will be relatively free of soil and microbial population will be limited to a few residual organisms that can be easily destroyed by a good disinfectant.

There are many good disinfectants on the market. However, only certain types are specific for the tubercle bacillus. A list of these can be obtained from the U. S. Department of Agriculture. In general, the phenolic type compounds are best. Cresol does a good job of destroying tubercle bacilli but may be objectionable due to a strong odor. Many phenolic formulations contain ortho phenyl phenol, which is more germicidal than cresol and has very little odor in use-dilution. Such preparations are preferable in dairy barns, poultry houses or for the treatment of poultry crates.

Where tuberculous contamination is not involved, hypochlorites are very effective disinfectants. The cleaned surfaces should be flushed with a solution containing 200 ppm. available chlorine.

Hypochlorites are cheap so liberal amounts can be used at a low cost. Either calcium hypochlorite which is marketed as a powder or sodium hypochlorite, a liquid can be used.

Good sanitation should always be practiced so that the cleaning and sanitizing process is easily accomplished. Although terminal cleaning and disinfection should be made if disease contamination has occurred, in all instances concurrent cleaning and disinfection should be practiced as a means of lessening the possibility of disease spread.

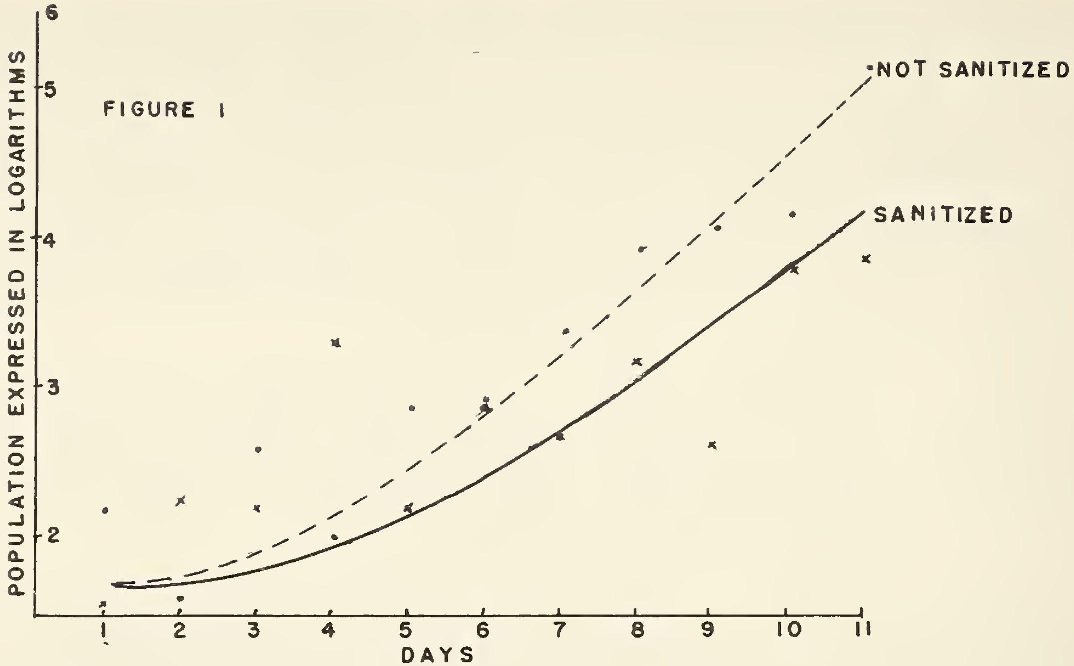
FIGURE 1
NOT SANITIZED
SANITIZED
POPULATION EXPRESSED IN LOGARITHMS
DAYS
6
5
4
3
2
1 2 3 4 5 6 7 8 9 10 11

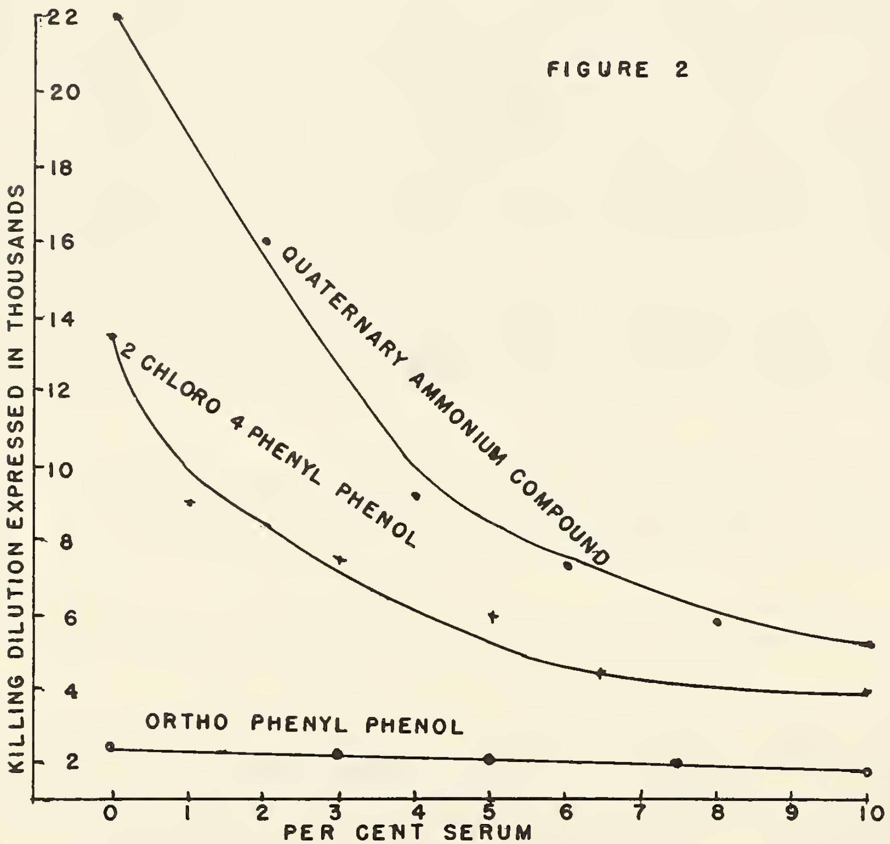
FIGURE 2
QUATERNARY AMMONIUM COMPOUND
2 CHLORO 4 PHENYL PHENOL
ORTHO PHENYL PHENOL
KILLING DILUTION EXPRESSED IN THOUSANDS
PER CENT SERUM
22 20 18 16 14 12 10 8 6 4 2
0 1 2 3 4 5 6 7 8 9 10

TUBERCULOSIS--A PROBLEM OF PHYSICIANS AND VETERINARIANS

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On November 15, 1957, I had the pleasure of attending the 61st Annual Meeting of the United States Livestock Sanitary Board in St. Louis, Mo., and the honor of having been invited for the fourth time to discuss the tuberculosis problem. My last title was: "Tuberculosis Eradication--Veterinarians Lead the Way." This title was chosen because it is a plain statement of fact. Eradication has been the goal of the veterinary profession and its allies, and at every turn it has far outdistanced physicians working in human medicine.

The veterinary profession has had certain advantages such as the short span of life of animals and permission to destroy the organisms on discovery along with the animals harboring them. More important than such items, however, has been the goal of eradication on a national basis visualized more than 40 years ago, and the continuous drive toward it without looking to the right or the left.

The world has never witnessed a finer demonstration of perseverance, patience, hard work, and complete confidence in attaining a goal than that exhibited by the veterinary profession and its allies in the effort to eradicate the tubercle bacillus.

All the more credit is due the profession when one realizes the formidable opposition it encountered. For example, in 1909 the Reference Handbook of the Medical Sciences carried the following statement: "No effective control of bovine tuberculosis is possible. To use the tuberculin test for its detection and to destroy all cattle which give the reaction would result in economic losses impossible for the State to meet."

For more than a quarter of a century before the eradication goal was set, the first kind of fundamental and practical research resulted in establishment of facts which revealed the natural history of tuberculosis in the animal body. This knowledge was essential if a successful eradication program were to be conducted. All fundamental information was transmitted to student and graduate veterinarians everywhere.

There was no place for theory, speculation, and the like because the facts were before their eyes. It had been known since 1882 that tuberculosis is caused by a microorganism. Before the 19th Century ended three pathogenic types--human, avian, and bovine--had been described. Prior to 1890, investigations revealed that accurate diagnosis was possible only by recovering tubercle bacilli. By the time organisms appear in the animal's secreta and excreta, the disease is usually advanced and contagious. Therefore, the diagnosis, although

accurate, was too late to prevent dissemination of tubercle bacilli to other animals.

With the advent of tuberculin in 1890, veterinarians were first to conduct extensive and well controlled research which determined its high degree of specificity in detecting the presence of tubercle bacilli in the animal body.

This research was so completely confirmed that informed veterinarians everywhere accepted the tuberculin reaction as proof of the presence of tuberculosis regardless of minuteness of lesions containing them. Thus, the profession accepted the tuberculin test as its sole diagnostic agent prior to the appearance of extensive disease and the presence of tubercle bacilli in secreta and excreta. Hence they were able to diagnose tuberculosis within approximately a month after the animal's body was initially invaded with tubercle bacilli, while the lesions were still microscopic and before the disease was contagious.

Observation revealed that healthy-appearing animals that reacted to the tuberculin test might at the moment, or at any subsequent time, have contagious lesions. Therefore, every tuberculin-reactor was looked upon as a reservoir of tubercle bacilli potentially capable of being spread among other animals and man. Inasmuch as no germicidal drug was available and no effective treatment was known, common sense dictated that all tubercle bacilli so found be destroyed with the animal.

So much research work was done, and the eradication method proved so efficacious that it was administered in a nationwide way beginning in 1917. Between then and now approximately 400,000,000 tuberculin tests have been administered to the cattle of this country and routine post mortem inspections have been made of the carcasses of more than 4,000,000 reactors. This is the largest well-organized project ever conducted anywhere at any time.

Nothing in life can even remotely be compared with experience. Having examined so many reactors at post mortem, veterinarians have much better information pertaining to the tuberculin test than any other group of workers including physicians in human medicine.

This is an exceedingly significant meeting in that your program extends through five days devoted to presentations on tuberculosis with a major emphasis upon the tuberculin test. It is all the more significant because you have reduced the incidence of tuberculin reactors so that only 0.156 percent of the 95,000,000 cattle of this country are infected with tubercle bacilli.

It is significant, too, because even with this low incidence you are trying to overcome complacency and push forward speedily to total eradication. This indicates an understanding of the real nature and problems of tuberculosis such as no other group of workers has ever manifested.

Recently I attended the annual meeting of the National Tuberculosis Association which derives its support from the sale of Tuberculosis Christmas Seals. A large number of fine papers were presented but with a disappointingly small percentage touching on tuberculosis.

Tonight I am to start attending the annual meeting of the American College of Chest Physicians in San Francisco, but the program lists less than 10 percent of the presentations on tuberculosis.

Such complacence seems almost unbelievable with approximately 33 percent (approximately 57,000,000) of our 173,000,000 people infected and a large crop of clinical and contagious lesions evolving annually.

The title you assigned me today is most pleasing since it provides an opportunity to emphasize how desperately every member of the veterinary profession is needed in the campaign to eradicate tubercle bacilli from people. Already veterinarians have eliminated a large block of tuberculosis from the citizens of the country by controlling the bovine type of tubercle bacilli in animals.

Despite all that the veterinary profession has learned by research and the information that is now available about tuberculosis in people, there is only a small handful of physicians, even among those working in the tuberculosis field, who have manifested interest in the natural history of the disease in the animal or human body. Probably this is the main reason for numerous theories, so much bickering, controversy, expression of personal opinion, and downright confusion about various aspects of tuberculosis in human beings.

One is reminded of John Godfrey Saxe's poem of the 19th Century entitled "The Blind Men and the Elephant". These six blind men of Indostan, each one in turn, were permitted to approach the elephant and examine the immediate area first touched. The first one contacted the side of the animal and described it as a wall. The second, a tusk, and said the animal was like a spear. The third, after touching the trunk, likened it to a snake. The fourth came in contact with the elephant's leg and described it as being like a tree. The fifth touched the ear and thought the animal was like a fan. The sixth grasped the animal's tail and said it was like a rope. The poem ends:

> "And so these six men of Indostan
> Disputed loud and long,
> Each in his own opinion
> Exceeding stiff and strong,
> Though each was partly in the right,
> All were in the wrong!"

Much of the confusion, controversy, etc. now existing in the minds of physicians of human medicine is due to lack of a clear understanding of the natural history of tuberculosis in the human body. There is so much talking and writing and sometimes final conclusions advanced from small segments in the natural history of the disease.

Too often such workers have touched only a small area of the disease. For example, one person's work may be limited to tuberculosis among children; he speaks and writes of what he sees, but with no correlation with the disease as it occurs in other periods of life. He observes large numbers of children who react to tuberculin, but with relatively little clinical disease. Therefore, he may conclude that the tuberculin reaction indicates the presence of protection against clinical disease.

Another individual devotes his time to hospital and sanatorium cases, most of whom have advanced disease, but he may have no conception of the natural history of tuberculosis leading to the advanced condition.

Another does only resectional surgery not realizing that excellent therapeutic results had been obtained long before surgery was introduced and not knowing the longrange effectiveness of resectional surgery.

Another may work largely in nutrition and attribute most beneficial results observed to diet. Still another may believe that only persons on long periods of strict bed rest recover, without knowing that large numbers of individuals have made good recovery without any treatment.

Another may observe sanatorium patients for four or five years after discharge and conclude that practically all relapses occur within the first two years without knowing that another 25 years of observation would produce more relapses than occurred in the first two years.

Another may fail to differentiate between primary and reinfection types of pulmonary infiltrates and treat both of them alike without knowing that nearly all demonstrable primary infiltrates subside regardless of how little or how much is done for them.

Still another may consider primary pulmonary infiltrates which may be in evidence about the time allergy is first demonstrable by the tuberculin test as the clinical type of tuberculosis and conclude that most of the clinical disease develops within two years after the initial invasion occurred not knowing that far more clinical tuberculosis appears later.

Without differentiation between primary infiltrate and reinfection type of lesions, erroneous deductions have been drawn regarding efficacy of therapeutic and preventive measures as well as relationship of degree of sensitivity to extent and activity of clinical disease. A number of other instances might be cited to emphasize that it is failure to become familiar with the entire natural history of tuberculosis in the human body and to report only from certain segments of it that causes so much confusion.

This situation is in no sense cited as criticism. Of necessity, many physicians have worked in limited fields where there has been no opportunity to correlate their findings with those working in other aspects of the disease. Many have had no opportunity to make longitudinal studies of

the patients whom they have diagnosed or treated. Some have worked only briefly in tuberculosis before transferring to other phases of medicine. Each is to be praised for contributing his observations through medical literature so that which pertains to different events in the natural history of the disease can be properly arranged. Only where this has been done have confusion and controversy been dispelled.

Veterinarians have been able to go directly to the lesions of tuberculous animals ranging from those recently invaded with tubercle bacilli to those dead from the disease. Thus the entire natural history was visualized leaving no place for personal opinion, theory, speculation, and therefore, confusion.

A recent panel was entitled "The Changing Status of the Tuberculin Test." The moderator, however, pointed out that the title might not have been well chosen and indicated that much that has been done and known may have been forgotten rather than that the status had changed. There is nothing new or no changed status about the tuberculin test. The public is becoming aware of its value so its use has greatly increased recently, but the test itself remains unchanged.

Apparently some physicians working in human tuberculosis have forgotten, and many others have not heard of, the fundamental research of a few decades ago which confirmed the specificity of the tuberculin test in people as veterinarians had previously established in animals.

For example, Anton Ghon, pathologist at St. Ann's Hospital, Vienna, by meticulous post mortem examination found lesions in all but one of the bodies of 184 children where the only evidence of tuberculosis during life was the tuberculin reaction. Examination was not completed on the body of the 184th child. Ghon's findings have been available since 1912.

The master key that unlocks every door leading to the eradication of the tubercle bacillus--the tuberculin test--has been tampered with so much with such erroneous deductions as to seriously discourage its use at many times and in numerous places. A number of persons have devised slightly different methods of administration designated by their names. Some have criticized standard dosage long in use with thoroughly proved efficacy. Various methods of preparing tuberculin have been employed with ardent followers for each method and much debate among their supporters.

Most of the controversies of the past, and the present, have been "much ado about nothing." Nevertheless, they have resulted in confusion in the minds of the citizenry. In fact, one frequently hears such questions as "What is tuberculin?", "What does the tuberculin reaction mean?", "Is there more than one way of giving the test?", "What is the difference between the kinds of tuberculin used in testing?", "Is it better to be a reactor than a non-reactor? I have heard that it is very dangerous to be a non-reactor."

At present, panel discussions and symposium are devoted to controversy at local, State, regional, and national medical, nursing and public health meetings. These have to do with whether Original Tuberculin (OT) or purified protein derivative (PPD) is the better testing material, the size of the dose administered, just how to read reactions when they occur and what a certain degree of reaction means.

Those who arrange such programs, as well as the participants, could be told by veterinarians that their questions were answered long ago and that their time would be much better spent in actual testing to locate tubercle bacilli and acting accordingly.

A physician may administer 100,000 or 1,000,000 tuberculin tests and read them 72 hours later. Those two procedures net no information whatsoever except the numbers who do and who do not react. Information concerning the importance of the tuberculin reaction in people, regardless of its degree, frequently cannot be obtained by immediate post mortem examination as is done in animals, but in general only by long-term observation and periodic examinations. A 10-year period of observation is too little and 25 years is still not enough for a life-time disease.

Numerous efforts have been made to correlate the degree of tuberculin reaction with extent and activity of clinical disease. Erroneous deductions have been drawn because the natural history of the disease in the human body was not considered. For example, it has been a matter of extensive and prolonged observation that when sensitivity develops following the initial invasion, it promptly reaches a high level. At this time from 5 to 8 percent of tuberculin converters present primary infiltrates large and dense enough and so located as to cast visible shadows on x-ray films.

Such shadows may be in evidence for a year or more and do not appear different from those cast by reinfection type of infiltrates. They are Ghon tubercles in the inflammatory stage. Unless this phenomenon of a high degree of allergy appearing and remaining over at least a few years and a demonstrable shadow-casting infiltrate being only of the primary type is understood, there is strong likelihood of such lesions being classified as active clinical disease.

Thus the erroneous deduction is drawn that those who have a high degree of allergy have clinical lesions more often than others. It is also well known that with passage of time allergy accompanying uncomplicated primary disease begins to wane and may decrease to such low level that it is not elicited by usual test doses of tuberculin.

Such errors can be pointed out by veterinarians who have gone directly to the lesions of tuberculin-reactor animals in various degrees of sensitivity. For the veterinarian to relate that necropsies on more than 4,000,000 animals with various degrees of sensitivity have revealed

no correlation between extent and progressiveness of clinical disease and degree of sensitivity, should sober those who would try to establish such a correlation based largely on such indirect evidence as x-ray shadows of lesions.

I can see expressions of amazement on your faces that there should be such confusion about a test for which the answers were provided so long ago. The situation would be amusing indeed were it not for the fact that the best opportunity of all time to eradicate tuberculosis is being overlooked. Just a few of the many questions asked by confused people have been mentioned to emphasize how important it is for veterinarians to become affiliated and participate actively in tuberculosis organizations. Experience of veterinarians is so large, and their accomplishments so great, that they can exert tremendous influence in eliminating from the minds of people so many erroneous concepts and thus help to dispel the present chaotic state.

By citing their own experience, which has resulted in marvelous accomplishments, veterinarians point out that the specificity of the tuberculin test was accepted on the basis of post mortem findings in reactor animals, that degree of reaction was found to have no relationship with extent or progressiveness of the disease.

The crying need for help from the veterinary profession at the moment is to convince physicians and the public everywhere of the absolute necessity of universal tuberculin testing, on as complete and periodic a scale as has been done and is being done among animals.

The continuity of method in the administration of the tuberculin test as used by veterinarians throughout their entire program should convince physicians and their allies in human medicine of the futility of adopting fads and fancies. Veterinarians have clung to Original Tuberculin (OT) with only one or two changes in medium since 1891. For approximately 40 years they have used essentially the same method of administration. Their accomplishments have long since proved their great wisdom in these respects and should convince those in human medicine of the futility of wavering from substance to substance and method to method.

No dependable immunity has ever been demonstrated in tuberculosis among people, therefore none of the numerous so-called immunizing agents has proved of avail. There is no premise for their use. Nevertheless, there is still much theorizing and speculation about immunity. Thousands of articles have appeared in the literature without adequate documentation of data, or sufficiently long observation of recipients, to justify the conclusions that have been drawn.

During the 11th annual meeting of the World Health Organization, held in Minneapolis this month a bulletin was issued on tuberculosis which contains the following: "Vaccination has prevented tuberculosis in millions of people and the new drugs have shown the possibility of its cure." There is not the slightest bit of well-documented evidence in reports from the

World Health Organization or any other source that BCG has prevented tuberculosis in a single person. On the contrary, there is an abundance of evidence in the medical literature of the harmful effects of this living tubercle bacillus to recipients. A more reliable statement from this organization was that tuberculosis remains the number one problem and this is true despite the extensive use of BCG.

The unfortunate dissemination of erroneous conclusions is due to the fact that in human tuberculosis laboratory workers and physicians have not been able to make meticulous, detailed examinations of the bodies of recipients during life and very few at post mortem, to obtain facts.

Veterinarians have done just this in countless instances, and by so doing have found all of the many so-called immunizing agents, including BCG, of no avail. Dissemination of these facts among our citizenry, which can be done best by veterinarians, would do much to stem waves of enthusiasm for such preparations as BCG promoted by persons who produce and dispense them.

Because BCG sensitizes tissues to tuberculoprotein, it nullifies the master key--the tuberculin test--to the eradication of the tubercle bacillus. This, in addition to its other detrimental qualities, such as producing clinical lesions in human bodies, would result in its total abandonment if the facts were brought to our citizenry everywhere.

At this moment there is much discussion among physicians about atypical tubercle bacilli and laudatory investigations are in progress. Until more is known about them and the part they play on the tuberculosis scene it appears unwise to enthuse about them to the point of overshadowing the three pathogenic forms so long known to be the significant offenders. Here again the experience of veterinarians can be used effectively.

They have demonstrated that sensitivity to tuberculin can result from dead tubercle bacilli and from some non-pathogenic types. Traum (1916), Daines, Crawford and others reported on tuberculin-reactor cattle with acid-fast organisms which did not correspond in any way with the well known pathogenic types of tubercle bacilli. They were recovered from nodules in the skin and were thought to be soil bacilli. It was also learned that human and avian types of tubercle bacilli which usually are not pathogenic for cattle could result in sensitivity. There is no reason to doubt that some acid-fast organisms not pathogenic for human tissues may also produce sensitivity in people.

Edwards and Palmer are studying a variety of tuberculins made from various atypical acid-fast organisms. The response to these preparations is compared with that of usual PPD in different population groups in certain parts of the country. In one area they have found that persons with low grade sensitivity to PPD present definitely stronger reactions to a preparation from one of the Batty atypical strains. One would expect that

nodules are produced by this bacillus from which it may be possible to obtain confirmatory evidence by recovery of the organism at post mortem or from biopsy material.

Long ago veterinarians introduced the term no lesion reactors for those animals in which lesions were not found at post mortem. Many believed lesions were present but were missed because of size or unusual location, thus the term no visible lesion reactor was substituted. The term no gross lesion reactor is now in vogue.

For such animals the term non-specific reactors was introduced implying that something other than bovine tubercle bacilli was responsible for the sensitivity. However, more extensive post mortem examinations on the carcasses of 1,000 such animals by Nassel revealed regular infections in 50.2 percent.

It has been suggested that still more meticulous necropsies such as Ghon did in children might bring to light a larger number. In all probability there would remain some whose sensitivity was not due to bovine tubercle bacilli but their number would be too small to be of much importance.

In people, as in animals, the term non-specific reactor has been employed. It has been suggested that reactions below a certain diameter be regarded as non-specific. This has not been generally accepted because degree of sensitivity caused by unmistakably pathogenic tubercle bacilli varies considerably from time to time. Moreover many cases are on record with slight or no reaction to the first dose of tuberculin, but with definite reaction to the second, who were found to have clinical tuberculosis. This has been observed in both acute and chronic disease.

There is little doubt that some non-pathogenic acid-fast bacilli cause sensitivity in animals and people but the problem of differential diagnosis awaits solution. Until a sound solution is found it seems safer by far to consider all characteristic reactors as harborers of pathogenic tubercle bacilli and act accordingly.

Prior to the opening of the 20th century, little was accomplished by way of tuberculosis control in people. Mortality and morbidity rates were high, and apparently most persons became infected with tubercle bacilli before the age of 20 years.

Early in this century two great movements were instituted which were largely responsible for this marked decrease in mortality, morbidity, and infection attack rates. One was the building of sanatoriums where persons with contagious tuberculosis could be isolated so they did not spread tubercle bacilli among others in their families and communities. Obviously, if children and others were protected against infection, they

could have no illness and death could not occur from tuberculosis. In this respect, the sanatorium soon proved its value.

The other great movement consisted of controlling the disease in animals, particularly cattle. Prior to this activity, large numbers of persons of various ages were infected with the bovine type of tubercle bacillus, which is just as destructive and killing in human tissues as in those of the bovine species.

Although much was done in certain localities to control bovine tuberculosis prior to 1917, the nation-wide campaign designed to eradicate it began that year and played a tremendous role in reducing the bovine type of tuberculosis in people.

The important role the control of tuberculosis in cattle played in this country becomes evident when one compares the incidence of bovine tuberculosis among people in parts of the world where the disease has not been well controlled among cattle. For example, in some places 50 to 65 percent of clinical, peripheral lymph node tuberculosis, about 50 percent of tuberculosis of the skin, 25 percent of meningitis and miliary disease, and 20 percent of tuberculosis of the genito-urinary organs and the skeletal system, and from 1 to 6 percent of the pulmonary disease in people has been found to be due to the bovine type.

Professor H. R. Smith has called attention to the marked decrease in incidence in certain forms of tuberculosis in people corresponding to the control of the disease in cattle. Therefore, the veterinary profession and its allies have thoroughly proved the value of their method of controlling the disease in animals and eliminating a large block of the disease in people.

The decline in mortality was precipitous and continuous after the sanatorium and tuberculosis eradication in animals movements got under way.

These two great movements set the stage for a third which is at least 25 years past due. They so reduced mortality, morbidity and infection attack rates among people that the third great movement should be directed at the tubercle bacillus itself rather than just trying to repair the damage it has caused. This field is now so overripe that a long leap toward the eradication goal could be made promptly. This consists of locating all people harboring tubercle bacilli and corralling their organisms.

When an attempt was being made to establish the U. S. Bureau of Animal Industry in 1883, the Hon. William H. Hatch of Missouri said: " . . . we find that in spite of the admitted fact that the most destructive diseases of people can never be thoroughly understood until more is known of the diseases of animals; in spite of the annual loss from preventable disease among animals in the United States, the

veterinary profession has been held in the background, discouraged and sneered at by those who should have assisted and defended it. Even in the Congress of the United States, which is supposed to represent the intelligence and the most progressive sentiment of the country, such terms of reproach and scorn as "horse doctor" and "scientific cranks" are hurled at those who are trying to prevent these enormous losses from falling on the livestock industry and to assist in throwing light on the most destructive plagues of the human race."

When the first Board of Health in the United States was organized in New York, a suggestion that a veterinarian be a member was received with ridicule and sarcasm. The idea that a veterinarian should be a member of an organization having for its objective the care of public health was treated as the wildest of absurdities. As late as 1907, when there was clamor for pasteurization in New York City, no veterinarian was appointed on the commission of five who investigated the danger of tuberculosis in dairy products.

As time passed, veterinarians demonstrated their tremendous value and, in some respects, have played a more important role in protecting the public health than physicians in human medicine. Tuberculosis is an example.

In 1935 Dr. Davis, Dean of the College of Medicine, University of Illinois, said: "The unity of veterinary and human medicine is a point of view accepted by all who understand the fundamental principles of diseases and their transmission . . . When we consider the large number of diseases common to man and the lower animals, it seems so necessary to dilate on this point. Many persons continue to maintain the point of view that human and veterinary medicine are separate fields of science largely because they grew up and developed separately and were practiced by different groups. This artificial distinction is unfortunate.

"Tuberculosis, for example, cannot be divided into human and bovine forms; the one to be studied and investigated by a veterinarian, the other by a physician, without sacrificing something."

Speaking before the annual meeting of the United States Livestock Sanitary Association in 1934, Morris Fishbein said: "The times have advanced so rapidly, as far as science is concerned, that any man who wants to keep abreast must be alert to the literature of his field. That means that your science is today a sister science to medicine in every sense of the word. It means greater and greater cooperation for the future if we are going to be able to do all that we can do together to stamp disease out of life, to make it possible to grow bigger and better animals, whether they are animals of a lower species or human beings, to make it possible to give them the maximum of life and service upon this earth." He pointed out that even then more than 1,000 magazines, bulletins, pamphlets, and reports on veterinary medicine are indexed regularly in the Index Veterinarius.

In 1920 Simon Flexner of the Rockefeller Institute for Medical Research said: "Our knowledge of yellow fever would in all likelihood have been delayed if the work of the Bureau of Animal Industry of the U. S. Department of

Agriculture on Texas Fever had not been done." Bang's work in brucellosis lead to excellent control measures for this disease both in animals and in people.

The eradication of such animal diseases as Texas tick fever, contagious pleural pneumonia, foot and mouth disease, and good control of rabies, brucellosis, trichinosis, and hog cholera, are among man's greatest accomplishments economically and health-wise.

Veterinarians are numbered among the world's most distinguished scientists. Many of our excellent research workers graduated in veterinary medicine including such persons as Dr. William H. Feldman, Dr. Karl F. Meyer, and Dr. A. G. Karlson. A considerable number of physicians who have made notable contributions began their careers and long worked with veterinarians, including Theobald Smith and M. P. Ravenel.

Some of the most famous physicians in human medicine have taken part in activities of veterinarians. A good example is Sir William Osler, who in 1870 began visiting veterinary hospitals probably because of his interest in comparative parasitology. Subsequently he had many intimate associations with the veterinarians at McGill University. Indeed, he was Professor of Physiology in the Montreal Veterinary College, and at one time was officer of the Montreal Veterinary Medical Association. He took great pride in his association with veterinarians and later published an article in the London Veterinary Review referring to his experiences as a former teacher in a veterinary school.

Inasmuch as each of the three main pathogenic types of tubercle bacilli produces disease in more than one species, and since they all cause clinical lesions in people, it is obvious that the eradication campaign must extend to all three types. In addition to causing disease in people, the human type also produces clinical lesions in such animals as swine, dogs, and parrots.

The avian type most often found in fowl also produces disease in swine, other domestic animals occasionally, and sometimes in man. The bovine type not only produces destructive disease in cattle but also in practically all other domestic animals, including pets such as dogs and cats, and is an incapacitator and killer of people.

There are examples of the futility of eradicating the one type without including the other two. For example, there are an ever-increasing number of cases being reported in areas where the bovine type of tubercule bacillus has nearly been eradicated from cattle only to be followed by animals becoming tuberculin reactors from infections acquired from people. Indeed periodic testing of cattle is now known as a good method of finding human cases of tuberculosis. This is not a new observation.

In fact, in 1895 Kinnell of Massachusetts said: "Affected animals are by no means the only source from which healthy ones contract the disease. We still have a constant supply from the diseased human subject against whom no quarantine restrictions have yet been devised." He said further: " . . .

until the medical profession can educate the public mind to an appreciation of the necessity of applying to diseased persons a degree of quarantine at least approximately equal to that enforced against diseased cows, there will be tuberculosis, and to spare, both among cows and among people."

While there are only slightly more than two dozen well-documented cases of clinical avian type tuberculosis reported in people, it is known that the avian type can be very destructive in swine and may result in tuberculin sensitivity in people and cattle.

The campaign of eradication therefore must be an all-out one. Hence veterinarians and physicians in human medicine must join hands in a universal attack against all pathogenic tubercle bacilli.

The veterinarian is as interested in seeing the human family freed from tuberculosis as the physician in human medicine since his health and that of his family are as much involved as those working in human medicine. Indeed, one of the main objectives of the veterinary profession in the tuberculosis eradication program among cattle has always been to protect people from this type of disease. Moreover, the veterinary profession is interested because its tuberculosis eradication goal will never be attained as long as there are infected owners and farm hands passing tuberculosis to cattle.

In addition to the National Tuberculosis Association, which derives its funds for fighting tuberculosis from the sale of Christmas Seals, and whose function is dissemination of information about tuberculosis everywhere, there are approximately 3,000 State and local affiliated associations and societies in this country. Indeed, they extend into every nook and cranny of the nation.

Unfortunately through most of the past, veterinarians have not had sufficient participation in these organizations. This also applies to State and local boards of health. If all veterinarians in America who have participated in the eradication of diseases from animals, particularly tuberculosis, were to become active members of these tuberculosis organizations, the whole tuberculosis eradication program could be prosecuted much more swiftly than at any previous time.

In the city of Columbus, Ohio, Dr. Arthur F. Schalk, Professor of Veterinary Preventive Medicine, Ohio State University, was appointed to the Board of Health in February, 1933, and was elected president two years later. He was reelected as president on at least one occasion. Concerning him and the policy of having veterinarians on the Board, the Commissioner of Health said: "We believe that to function properly it is essential that one member be an authority on veterinary medicine."

James H. Steele, D.V.M. is now employed by the United States Public Health Service under the title of Chief of Veterinary Public Health. He plays an important role in those diseases transmissable from animals to man and vice versa.

Physicians in human medicine should publish frequent articles in veterinary journals and bulletins so as to keep veterinarians everywhere informed of the tuberculosis problem among people. To a greater extent, veterinarians should publish articles in medical, nursing, public health, and other educational journals calling attention to their phenomenal accomplishments, how they were achieved, and what remains to be done. Such articles are extremely valuable to physicians, nurses, and all others concerned in the public health.

Some of this is being done to fine advantage. For example, in 1946 the American College of Chest Physicians invited H. M. O'Rear, D.V.M., Sacramento, to present a paper on "Hazards of Bovine Tuberculosis as a Matter of Public Health Significance and Potential Human Lung Infection with Bovine Tubercle Bacilli". This was well received and was later published in Diseases of the Chest.

Dr. James H. Steele accepted an invitation to read a paper entitled "Animal Tuberculosis" before the annual meeting of the National Tuberculosis Association in May, 1957. This paper is scheduled for publication in the American Review of Tuberculosis and Pulmonary Diseases.

Dr. Paul S. Dodd, County Veterinarian at Danville, Illinois, had a most enlightening article in the April, 1958, issue of Journal-Lancet and another on the "Bovine Tuberculin Test" in the April, 1958, issue of the Bulletin of the National Tuberculosis Association. Dr. A. F. Ranney and Dr. Ralph L. West, Executive Secretary, Minnesota State Livestock Sanitary Board, have most informative articles on bovine tuberculosis soon to appear in Diseases of the Chest, which is an international journal with subscribers in 89 nations and territories. It would also be helpful if veterinarians everywhere would write letters frequently for columns such as "What Everybody Thinks" appearing in weekly and daily newspapers.

The Illinois Tuberculosis Association has long recognized the great importance of enlisting the support and the participation of veterinarians in its tuberculosis activities. For example, Dr. Paul S. Dodd, County Veterinarian at Danville, Illinois, has served on various committees, and in 1957 was president of the organization. All through the years, he has contributed mightily to the tuberculosis eradication program both in animals and in people.

The Montana Tuberculosis Association arranged a symposium under the title "Present Status of Animal Tuberculosis". This was presented by four veterinarians before the annual meeting of the Montana Tuberculosis Association in April, 1958.

For many years, I have looked upon Professor H. R. Smith as one of America's fine contributors to the health of both animals and people. He has played such a prominent role in assembling and analyzing data and disseminating the facts obtained as to have been extremely influential in bringing about legislation, appropriation of funds, stimulation of interest and activity in the tuberculosis eradication movement among animals. His name and work well deserve an important place when the final history of the eradication of tuberculosis is written.

For so many years, I have been in close touch with him through frequent communication and meetings. He has always been such a veritable storehouse of information that I had hoped some day he would prepare an historical sketch of the cattle tuberculosis eradication movement. This he has now done and his booklet, as he calls it, under the title of "The Conquest of Bovine Tuberculosis in the United States" is now off the press. I had the honor of reading the manuscript before publication and have since read the book.

This book deserves exceedingly wide distribution. There are many people who have forgotten the former seriousness of tuberculosis among animals and many among the younger generations may not have heard of it. It behooves our professions to promote the dissemination of this book everywhere, especially among the youth of America to whom it is dedicated. Professor Smith not only presents the history of the eradication movement among animals, but points out the importance of universal testing of people with tuberculin.

One may wonder if an important reason for veterinarians not entering the program to eradicate tuberculosis from people has been the confusion about various aspects of the disease which for so long resulted in a situation that appeared so hopeless.

For example, reports have revealed that approximately three-fourths of diagnoses are made after the disease is in an advanced stage when long periods of hospitalization and incapacity for life were the fate of many. And many clinical cases are developing with almost no effort to detect the disease promptly after invasions of tubercle bacilli occur.

Unfortunately this situation still prevails in some places, but the solution of the problem is known and only awaits more general acceptance and practice. Extensive and prolonged studies of sufficiently large groups to justify conclusions have revealed that periodic examinations of persons who react to tuberculin will usually detect evolving clinical lesions while in the pre-symptom, pre-contagious and easily treatable stage.

It is known that tuberculin-reactor children rarely develop chronic pulmonary tuberculosis. Their chronic lesions are far more likely to appear extrathoracicly, in such parts as lymph nodes, joints, etc. A very small percentage of children who react to tuberculin develop acute reinfection forms of the disease including meningitis, pneumonia, and miliary tuberculosis. Therefore each infant and child who reacts to tuberculin should be kept under observation for these conditions for which treatment is now available.

As adolescence approaches and thereafter throughout life, chronic reinfection type of pulmonary tuberculosis becomes the predominant form of the disease. It is usually slow in its evolution and is readily detectable after it becomes sufficiently gross and has consistency to cast x-ray shadows.

In fact, when periodic x-ray films of the chest are made at sufficiently close intervals (at least annually) of tuberculin reactors among adolescents and all who are older, 95 percent of evolving chronic lesions develop qualities to cast visible shadows on x-ray films on an average of more than two years before they produced symptoms or become contagious. Moreover, when found at this time, almost all such lesions can be treated successfully with little loss of working capacity and in a relatively short period.

If one waits until symptoms appear, approximately 85 percent of chronic lesions are in an advanced stage when found. Usually they are then contagious. The all-out mass x-ray survey is unsatisfactory in this respect because it cannot be repeated with sufficient frequency. Between surveys lesions can appear, become advanced, contagious, and even kill. Therefore the only sound approach is to find the disease first by the tuberculin reaction and make periodic examinations including x-ray films of the chest much more often than is possible in mass x-ray surveys. Thus tubercle bacilli are stymied because they are denied the opportunity of sending out their progeny to infect other people and animals. Thereafter it is a matter of keeping them corralled in the human bodies they inhabit.

We are still unfortunate in not having a drug that will destroy tubercle bacilli in the human body. Our present drugs are suppressive and are of great value, but they do not cure tuberculosis. However, there is reason to believe we may be on the verge of having a germicidal drug. If so, it is only periodic testing with tuberculin that will determine when that drug can serve its purpose. It must be administered as soon as possible after the invasion with tubercle bacilli has occurred and nothing but the tuberculin test provides such information.

The blood supply of many tuberculous lesions is soon lost after which it could hardly be expected that even highly germicidal drugs in the blood stream could reach tubercle bacilli in avascular necrotic areas. Before this loss of blood supply has occurred, lesions usually are small and vascular and one might expect to destroy all tubercle bacilli in a human body with a truly germicidal drug.

Therefore physicians in human medicine now have satisfactory armamentarium for the solution of the tuberculosis problem in people. However, the effectiveness of this method depends upon making the entire citizenry aware of it to such a degree as to demand its use. Barriers must be broken down between professions, organizations, and individuals, for an all-out attack on the tubercle bacillus regardless of its type. Personal opinion, speculation, unimportant minutia, have no place. They have been outlawed by well established methods based on facts which make success certain wherever applied.

The total eradication goal will be approached most swiftly when veterinarians and physicians in human medicine and their allies unite in a common effort to eradicate pathogenic forms of tubercle bacilli from people and all animal species.

OVERCOMING COMPLACENCY IN OUR ERADICATION PROGRAMS

C. Donald Van Houweling, Office of the Administrator
ARS, USDA, Washington, D. C.

I appreciate more than I can tell the opportunity of being here and hearing the fine talks such as we had this morning and to get to take in some more of the conference before I have to leave. I sincerely appreciate the invitation that the program arrangers have given to me to speak to you. I think it is quite a compliment.

I hope you don't all have the same experience that I do, but occasionally at home, where I have my severest critics, I am taken down a peg or two. Last Sunday, around the dinner table, my boy said to me "Where are you going this week, Dad?" and I said, "I'm going out to East Lansing, Michigan." "What for?" he asked. "They are having a Tuberculosis Eradication Conference out there," I replied, and my teenage son came back with, "Oh, you're going out to learn something, are you?" I said, "Yes, I will, but I want you to know that I'm one of the speakers, I'm part of the staff." He says, "Huh, what can you teach them about tuberculosis with all those experts out there?" Finally I said, "Well, I can't teach them a thing about the technical aspect of tuberculosis, but maybe that's not the most important part of tuberculosis eradication now. Maybe some of it depends on our mental attitude and the frame of mind, the philosophy that we have in regard to this program. And that happens to be what I have to talk about." So, that is why I am here.

I want to take this opportunity to express to Michigan State University and Dean Armistead and his staff, on behalf of the Agricultural Research Service and the Animal Disease Eradication Division, our sincere thanks to you for the excellent cooperation that we have received from this institution. I think this is the third or fourth conference similar to this that we have put on in cooperation with you. Each one is well received and each time we get nothing but the finest reports on the cooperation that we receive from the entire staff. We appreciate very much this fine help. I also want to take this opportunity to thank the speakers outside of our own staff who have taken time from their very busy schedules to prepare talks and to come and be with us here at this time.

We're grateful to all of you. And I think every one who has looked over this program would want to express with me their congratulations to those who have arranged the program. It is chuckfull of fine discussions and demonstrations. These can be attributed, I think, to Dr. Winter and his staff, and, again, to Dr. Armistead, Dr. Scott, and others who have arranged this program.

I know it is going to be extremely beneficial. We're depending on it to really do something big for our tuberculosis eradication program. I'm sure it is something that we have needed for quite some time, and I hope that it will be the beginning of an increased emphasis on tuberculosis eradication in this country, perhaps even a new look at this whole program.

We are not the least bit like the woman I heard of who went to see her physician and complained because her son was showing symptoms of extreme nervousness and seemed to be too jittery and excitable. As the physician looked her over and discussed her son's case he noticed that she was a little bit twitchy, too, that she jittered and that she couldn't sit still. He thought perhaps he should help her first, so he prescribed one or two common tranquilizer pills. She happened to see him on the street a few days later and he said, "Well, how is your son doing?" Her response was, "Who cares?" That certainly is not our attitude in regard to tuberculosis eradication.

Now the dictionary defines complacency as: contentment, satisfaction, especially self-satisfaction. Back in March, I attended an Alabama State Veterinary Medical Association meeting, where we had a joint work conference of State and Federal veterinarians. Since I had to leave soon after the conference started, they gave me a chance to speak to the group first. I started talking a little bit about tuberculosis, commenting that I thought we still had a problem in tuberculosis eradication. We got a little bit of discussion back and forth, and finally one of the older fellows in the group said, "Please, excuse me, but let's quit talking about TB and talk about Bangs. We've got a lot more of that."

Now I wonder if that isn't pretty typical of the attitude of a lot of our people? Many of you have attended the meetings of the United States Livestock Sanitary Association and I'm sure you have been impressed as I have. In recent years the TB committee meets and, if they are lucky, there are perhaps a dozen people there. In comparison, when the brucellosis committee meets you need a room as big as this. We don't have one meeting; instead we have three sessions. They start at eight and maybe they go to twelve or one o'clock to give everyone a chance to express himself.

Maybe that is indicative of our attitude in regard to tuberculosis. I'm afraid our attitude in regard to accreditation and reaccreditation of counties is that we've been inclined in the last few years, starting about 1940, to think in terms of how little can we do and still maintain accreditation. I'm sure you all agree that isn't the way to achieve eradication.

I don't know when there has been a meeting of the livestock industry in the last 10 years when tuberculosis was the main subject of discussion. And I go to quite a few. While on the subject of brucellosis, we can wax loud and eloquent at the many meetings where it is featured. Maybe we're starting to get some of those things said.

I can't recall in the four years that I spent at Iowa State College ever seeing a tuberculin test applied to an animal. If we were shown, I can't recall it, and I'm sure I didn't have the opportunity to do it myself. And I think this was the condition that existed for several years.

Maybe that is an indication of what our attitude has been, and perhaps we are now reaping the results of that kind of attitude. And I'm afraid in too many cases, our attitude today, our view in regard to tuberculosis, is expressed by the following expression: "It's a lot of work to eradicate tuberculosis." I say to you, of course it is. I don't think anything worthwhile has ever been done that wasn't a lot of work. Another one we hear is "We only want to keep it under control" Some people have asked whether we have reached the irreducible minimum in tuberculosis eradication. The only thing I can say in regard to that statement is, have we forsaken our goal of eradication?

Another thing we hear is that testing techniques are not very important after all. Our men have been applying this test for 40 years. They know how to test these cows. You don't have to have them restrained, they can do it on the run. I would ask these very distinguished scientists here whether there is any biological test in which techniques are not important. Is there any test that you could do in a slip-shod, half-hearted manner and get uniform, consistent results.

Another thing we hear is that you just can't trace every case of tuberculosis. And still we have too many States that are refusing to try to use one of the tools that has been offered, the uniform or national eartagging plan which we feel would be a real benefit if we could all apply it.

Another thing we hear so often is that NVL's or NGL's are not tuberculosis. We've gotten to the point where some of us are putting more reliance on post mortem findings than we are on the tuberculin test, and I don't believe we could have got to where we were in 1940 if that had been the program.

Another thing we hear so often is that you can't identify all livestock going through markets. You lose them, and can't possibly keep up with them. We've been doing some trial work

in that regard. I believe we can give some answers and some help on this problem of identifying livestock through markets.

Some of our people have been making a study of this and we find out, first of all, we don't know which is the best tag to use. We must perfect that. So we have a long way to go before we can throw our hands up and say we can't do that. And then the last one is, and I hear this every once in a while, "We can't eradicate tuberculosis, we're just going to have to live with it." Now the only purpose is bringing out all these attitudes, I suppose, is to sort of take stock of where we are and then ask you how we overcome this attitude.

I think it is important that we recognize that the first big job we have to do is reverse the frame of mind that we have developed. Someone has said, "Disease eradication is a frame of mind. In Canada, they don't have hog cholera; in England, they don't have rabies; we don't have foot-and-mouth disease in the United States, and it is only when we determine to live without diseases that we can eradicate them."

Now, how do we change this nebulous thing that might be called the "frame of mind"? First of all, I guess we have to dig out the old facts, dig out some new facts, then we have to present them in a way so that everyone can understand and utilize them. We must get these facts across to veterinarians and to livestock producers all over the country.

I'm afraid it won't be adequate for just the group gathered here to get the story. It won't be adequate for just full time State and Federally employed veterinarians to get the story. We're going to have to convince all veterinarians.

There's a whole crop now just like myself who didn't get much training for 10 or 15 years on tuberculosis tests. Then, we must finally have a really aggressive action program of eradication based upon these facts and the tools that we have at our disposal.

In regard to the question, "Can tuberculosis be eradicated?" the thing I always come back to when I hear that question is that if foot-and-mouth disease could be eradicated from the United States nine times, from Canada once, and from Mexico twice, and if it looks now like vesicular exanthema has been eradicated from the United States, and if we were able to eradicate the fever tick from the United States, I think tuberculosis, too, can be eliminated. I don't think we can say that it can't be eliminated until we have really tried. And I don't believe that we can say we have really tried up to now.

So what do we need to do? First of all, I think perhaps the most important thing is to agree once again that it can be done, then reestablish confidence in the tuberculin test. Before we discard it let's be sure that we have ruled out some of the other factors that may be confus ing the problem.

Before we say that we don't have tuberculosis in the herd because we are apparently getting non-specific reactions or don't find lesions on post-mortem, let's rule out the possibility of avian sensitization, human sensitization, and Johnes disease. Until we rule out those factors I don't think that we should discard the reliability of the tuberculin test. And this hasn't been done all over the country. We have to recognize, too, that technique is an important part of the eradication program. I think I've said enough about that but if this is a scientific test, a biological test, if there are proven ways to apply and interpret it, let's get that uniform procedure in its application and interpretation and make the best use of it we can.

I think we do have to do a better job of identifying animals so they can be traced, and I think we have to reorganize, perhaps, or at least organize again to eradicate, not just to control, and then never be satisfied until tuberculosis in cattle, and in the other animals, is eliminated.

So which way are we going? Are we going to sit back after this meeting and say it was a fine meeting? Are we going to agree that we have had a wonderful lot of papers, good, inspiring speeches, wonderful demonstrations, and then sit back and say it just can't be done? If it is, I think we may just as well call this meeting off and go home right now.

What must we do if we are going to succeed in this program? I think it can be boiled down to about three basic principles. First of all, when we have found reactors, the herd of origin must be located so that every animal can be tested. Secondly, when we have an outbreak, we must establish the source of the outbreak, use sound epidemiological principles, and dig in until we have established the source of the infection. We have some plans to improve that service. We must keep infected herds under quarantine and surveillance and not to let them go too soon.

I think there are records enough to show that these herds have a way of continuing to be found for years and years and that maybe we haven't done quite well enough in keeping them under quarantine and under surveillance.

I think that it is highly important to be able to trace all infected animals and to know that you have reached all those that have been exposed, to establish the source of your outbreak, and lastly to maintain quarantine and surveillance -- and never to assume. We should never assume any of these things because when you assume you're too apt to make asses out of you and me.

TUBERCULOSIS ERADICATION IN CANADA

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The first tuberculin tests were carried out in Canada about 1900. At this time free tests were applied to Canadian herds and to imported and exported animals.

The first plan to eradicate tuberculosis was adopted in 1913. It was known as the Supervised Herd Plan, and under this plan owners could have an annual herd test without charge. Reactors were marked and removed from the herd without compensation. This was a voluntary plan which was discontinued in 1952 when all of Canada came under the compulsory Restricted Area Plan.

About 1914, municipal by-laws were passed in many cities which compelled shippers of whole milk to have their herds tested. As a result, the municipal tuberculosis order was passed to qualify these herds. The first compensation for reactors was paid under this plan.

In 1919 the Accredited Herd Plan was formulated for herds of purebred cattle only. This was desirable since owners of purebred cattle were continually selling herd sires and foundation breeding stock.

The testing of cattle on an area basis was commenced in 1923 under the Restricted Area Plan. Under this program a majority of two-thirds of the cattle owners in an area must be in favor of this plan. Then the Provincial Minister of Agriculture asks the Federal Minister of Agriculture to constitute a defined area as a Restricted Area.

In Restricted Areas the testing of all cattle in the area is mandatory and reactors must be slaughtered. When the reactors are removed from the herd, the owner must clean and disinfect his premises following which he receives compensation from the Federal Government. This plan provides for the controlled movement of cattle into an area, which prevents the introduction of infected animals.

At the present time we have only two policies, namely, the Accredited Herd Plan and the Restricted Herd Plan. We have almost 10,000 herds comprising 450,000 cattle under the Accredited Plan and all of Canada is a Restricted Area.

The Accredited Herd Plan is a voluntary plan available only to owners who have a minimum of 10 purebred cattle of one breed and the number of purebreds in the herd must comprise at least half the total number of cattle in the herd. We also require adequate lighting in the barn, good sanitary conditions and facilities for the isolation of additions.

For acceptance under this program we have made our standards high, since the plan is intended only for bona fide breeders and since we favor the Restricted Area Plan. All tests are conducted under the Accredited Herd Plan at the expense of the Federal Government by full-time salaried veterinarians or practitioners employed on a casual basis.

When a herd meets the requirements the owner signs an agreement that he will comply with all the regulations. The herd is then submitted to a combined tuberculin test using the high and low intradermal injection. Our officer also makes a careful physical examination of the herd. If this test is negative the herd is retested in one year with a single intradermal tuberculin test. However, herds which have passed a negative test under the Restricted Area Plan before acceptance under the Accredited Herd Plan are retested in six months.

When a herd has passed the required negative tests, an Accredited Herd Certificate is issued to the owner and the herd is known as a fully Accredited Herd. These herds are retested annually, and if negative the Accredited Herd Certificate is renewed. If infection is uncovered in a fully Accredited Herd it must pass a 60-day and one semi-annual retest to again attain full Accredited Herd status.

In Accredited Herds all milk and dairy products fed to calves must be from an Accredited Herd or must have been pasteurized by heating to not less than 150°F for not less than 20 minutes.

All additions to Accredited Herds must be isolated pending a 60-day retest except additions from another fully Accredited Herd.

I will now describe our Restricted Area Program. When a Restricted Area is constituted by law, the plan is mandatory for all owners within the area. All cattle, including calves, are tested by a full-time salaried officer or a practitioner employed on a casual basis and there is no expense to the owner for testing. Owners of cattle, when requested by our inspector, must assemble their animals for testing and provide whatever additional help may be required.

When all the cattle, including calves, have been tested in a county or in a municipality, the area may be accredited for three years provided the percentage of infection was not more than one-half of one percent. The area may be accredited for six years if the percentage of infection was not more than two-tenths of one percent and at the end of this period the accreditation of the area may be extended for three years if there is no indication that tuberculosis is increasing.

In areas where the infection is over one-half of one percent but not more than one percent the area may be accredited for three years provided the infected herds are retested and as a result of this retest the infection in the area is not more than one-half of one percent of the total

cattle population. Our regulations also provide for the accreditation for three years when cattle are tested under range or semi-range conditions.

We have a few areas in Western Canada tested under the range privilege. In these areas we test all bulls, purebred breeding animals, milk cows, home-fed cattle and at least 10 percent of the range or semi-range cattle. If a reactor is found in these cattle we submit the entire herd to a test.

Additions are permitted entry into the area provided they are from Accredited Herds or another Restricted Area which has undergone at least one test. Cattle from untested areas coming into the Restricted Area on a permanent basis are only permitted entry when the herd of origin has passed a negative herd test within the previous 12 months and the cattle entering the area have passed a negative tuberculin test within 60 days. There is an exception for feeder cattle which may enter an area under licence. They must be kept isolated pending a negative test on the purchaser's premises. There is no provision for the payment of compensation for feeder cattle tested under these conditions.

We also have certain stockyards exempt from the Restricted Area Regulations for the assembling and marketing of cattle. Breeding cattle are permitted to enter an area from these stockyards after passing a negative test at the stockyards. These cattle are isolated on the purchaser's premises within the area pending a retest in 60 days.

We require infected herds in Restricted Areas to pass a negative 60-day retest and two semi-annuals before they attain area status.

Many of our requirements apply to our two eradication programs. Reactors must be shipped without delay. We try to have all reactors slaughtered within two weeks from the date they are uncovered and we insist that they be slaughtered within 30 days. Reactors are slaughtered at abattoirs under Federal veterinary inspection. However, in remote areas or when an animal has sustained an injury we will permit a veterinarian to conduct a post mortem on the farm. In these cases infected portions or carcasses must be disposed of by burning or deep burial, and under no circumstances can they be released for animal food.

All the compensation received by the owner is paid by the Federal Government. The Animal Contagious Diseases Act is the authority for this payment. The maximum compensation for purebred animals is $100 and grade animals $40, which we refer to as field compensation. The owner, of course, receives the salvage value of the carcass from the abattoir. If the carcass is condemned as unfit for food, the Government pays in addition to the field compensation the value of the carcass if it had been passed for food. Compensation is not paid until the owner has completed a thorough cleaning and disinfection of his premises.

Under the Animal Contagious Diseases Act we can only pay compensation for animals ordered slaughtered and these animals must have been slaughtered under veterinary inspection. When a reactor dies before slaughter the owner may be compensated through the Supplementary Estimates voted by Parliament.

Supplementary compensation also applies when tubercular lesions are found in an animal in a Restricted Area where a post mortem examination is being conducted for any purpose. The diagnosis must be confirmed by laboratory examination. Supplementary compensation also applies when a non-reactor animal is condemned for tuberculosis at an abattoir providing the owner did not receive payment for the carcass from the firm. In these cases the diagnosis must also be confirmed by laboratory examination.

We insist that the owner thoroughly cleanse and disinfect his premises following the removal of reactors. We instruct the owner to remove all litter and manure from the stable and vicinity of the buildings. The entire stable must be cleaned by washing and scrubbing, preferably with lye and a hot water solution. We then instruct the owner to apply to the interior of the stable an even, heavy coating of limewash with an added coal tar disinfectant which will form a homogeneous solution with the limewash.

Our inspector instructs the owner on the procedure which he must follow. We believe that the application of limewash is important since it indelibly marks the region that has been treated and in addition physically seals in and destroys the micro-organisms. All manure must be removed from the vicinity of the buildings. When the work is finished our inspector visits the premises to determine whether or not the work was done satisfactorily.

When reactors are found in any herd we find out the owners' sales and purchases over the past two years. All herds from which reactor animals originate and all animals sold for breeding purposes are submitted to a special retest.

Our tuberculin readings are conducted at the 72nd hour except in problem herds where we often conduct readings at the 72nd and 96th hour. All animals injected with tuberculin are ear tagged at the time of the injection. This applies to all animals in the herd including calves. Reactors are identified with red ear tags in the left ear. This ear tag has the word reactor stamped on the upper side of it.

We deal with problem herds by having our officer carry out a careful physical examination of the herd as well as applying special tests. The evidence or history of infection in other farm animals such as poultry and swine is investigated. Special attention is given to the cleaning and disinfection procedure, contact with other cattle and the feeding of livestock products. In these herds we have used the double intradermal test,

cervical test, subcutaneous test and also the opthalmic test. We recommend the subcutaneous test in herds which continue to reveal no visible lesion cases.

Where there is no history of infection in Accredited Herds or on a general retest of a Restricted Area, we permit our officers to quarantine animals with non-specific reactions. These animals are isolated and retested in 60 days, at which time a decision must be made as no further retests are permitted.

Skin lesions have been a problem in many countries. In Canada, cattle with skin lestions which react to the tuberculin test must be classed as reactors since they may have lesions of tuberculosis in other parts of the body. With valuable animals we have given the owner the privilge of having skin lesions removed by surgery. Under these circumstances the animal is quarantined for a 60-day retest and many of these animals are negative at the retest.

In carrying out the intradermal test in the caudal fold we instruct our officers to inject mid-way along the ventral border of the right caudal fold. The left fold is used as a control. Before the animal is injected the site of the injection must be cleaned with absorbent cotton moistened with ether or alcohol and then one-tenth of a cubic centimeter of tuberculin is injected with an intradermal syringe.

Great care must be taken to see that the injection is made intradermally between the epidermis and the corium. The tissue must not be traumatized by rough handling or careless injection of tuberculin. Following injection it should be possible to feel the injected tuberculin in the skin in the form of a definite bleb.

A negative reaction is one in which there is no change in the tissue at the point of injection. A positive reaction consists of a circumscribed tumefaction, induration or diffuse swelling of the tissue at the sight of injection. A non-specific or suspicious reaction is any appreciable disturbance at the sight of injection but which does not reveal the characteristic indications of a positive reaction.

Animals showing no reaction are recorded as negative. Circumscribed swellings pea size (diameter 3/16") are used as a basic standard and designated as P1. Larger swellings are recorded as P2, P3, P4 and P5, etc. For diffuse swelling in which injected caudal fold is twice as thick as the normal fold the reaction is recorded as T2. Larger swellings are recorded as T3, T4, etc.

We feel that the proper application and interpretation of the tuberculin test is of paramount importance. Senior officers train all newly appointed full-time veterinarians for one month on general work which must include a thorough training on tuberculosis.

Before accredited veterinarians and practitioners employed on a casual basis can conduct tests they must receive four days' training on the application and four days' training on the interpretation of the tuberculin test. This training must be done by a senior veterinarian who has had wide experience. Wherever possible new appointees observe tuberculin reactions in the field even though it may necessitate travelling a considerable distance.

Because of the decrease in the incidence of tuberculosis, it is sometimes impossible to demonstrate tuberculin reactions in the field. To overcome this we have, during the past few years, sensitized cattle with dead organisms and later demonstrated the tuberculin test on these animals. We have arranged to do this every year at our two veterinary colleges, which will give each graduate an opportunity to be familiar with the test and will prepare him for further field training if he is engaged in this work.

In addition to adequate training we have found that the proper supervision of field personnel is essential. This is done by a senior officer accompanying the veterinarian who is conducting tests. The supervising officer can observe the application and interpretation of the test and give instructions on the proper procedure. The best appraisal of this work can be made when the supervisor makes unannounced visits.

All areas in Canada have now been tested at least once except small portions of Alberta and Saskatchewan and also a few outposts in Newfoundland. Our Tuberculosis Eradication Policy has reduced the incidence of tuberculosis from a high of 20 percent in some areas at the initial test to a low of 0.14, which is the percentage of reactors uncovered in the last fiscal year.

We conducted about 1.5 million tuberculin tests in the last fiscal year. The number of carcasses condemned on post mortem has, of course, decreased and the number of no-visible-lesion cases increased to 47 percent. We are not surprised at the number of no-visible-lesion cases since we must expect the number to increase as we continue to eradicate this disease.

We in Canada have always felt that we must continue to retest all cattle in an area when the accreditation expires even though the percentage of infection at the previous test was negligible.

We believe that the tracing of non-reactor cattle which have lesions of tuberculosis on post mortem is essential in our eradication policy and we can trace most of these animals with our system of ear tagging.

"Health of Animals" ear tags are used to identify all cattle tested for tuberculosis or brucellosis. These tags are all purchased by the Federal Government. We code them by districts which enables us to

immediately identify the district where the tag was used irrespective of where the non-reactor was slaughtered.

These tags are then distributed to our sub-district offices and a certain series is assigned to each sub-district. Our sub-district offices embrace several counties. When the tags are given to individual inspectors they are instructed to use the tags consecutively, and when a county is completed all tags which have not been used are turned in to the sub-district office.

By this procedure we can quickly find out the county where the tag was used. To identify the herd owner we have our field officers record the tag numbers used on each owner's premises. This list is sent to the sub-district office with his weekly totals. Subsequently these numbers are recorded consecutively with the owner's name opposite the ear tag numbers.

Although it is more cumbersome, we can trace calfhood vaccination ear tags. These ear tags are purchased by the Provinces and distributed to the practitioners. When an animal does not have an identification tag we find out from the abattoir the lot number of the kill. The abattoirs in Canada slaughter cattle by lots which are usually made up of cattle from about 12 owners. Sometimes cattle are consigned in a drover's name and when this occurs we have to find out from the drover where he purchased the animals. This method of tracing is difficult and it usually means testing 12 or 15 herds to find the herd from which the non-reactor originated.

When hogs are condemned for generalized tuberculosis in our packing plants, we find out the owner's name and test his cattle, since we have often found tuberculosis in the cattle in these cases. In Canada all hogs are graded on the rail; they are identified by tattoo and it is easy to find the owner.

Since Canada is particularly interested in the export of cattle to the United States, we take every precaution to ensure that only animals free from tuberculosis are shipped. Most of this work is done by our accredited veterinarians who receive a thorough training in the application and interpretation of the tuberculin test before we accept their health charts for endorsement.

Senior full-time salaried veterinarians closely supervise this work by making unannounced visits to accompany accredited veterinarians on reading days. When an accredited veterinarian has injected cattle for export he must immediatel notify our sub-district veterinarian who is then aware of all cattle under test for export.

We are very careful to identify each animal in order that we will know whether or not the animal is from a herd of accredited area status. Cattle moved from one sub-district to another are accompanied by a tuberculosis and brucellosis health certificate.

Although we encounter many problems in the eradication of bovine tuberculosis we are convinced that we will eventually eradicate the disease.

AVIAN TUBERCULOSIS AND ITS RELATIONSHIP TO BOVINE TUBERCULOSIS ERADICATION

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It is, I believe, significant that those who planned the program for this conference envisaged the oneness of the tuberculosis problem. Although the problem consists of many facets, these facets constitute an indivisible whole.

Man, cattle, chickens, and voles are the only natural hosts for the four recognized types or varieties of tubercle bacilli. Phylogenetically, the different species which may and do serve as foreign hosts constitute an impressive list. For this reason a successful program for eradication of tuberculosis must include an attack on the disease wherever it occurs. The elimination of tuberculosis from one species, even from man, would not notably affect the occurrence of the disease in chickens, in cattle, or in swine. A united and continuing attack on tuberculosis in all species is the only way to achieve the final conquest of this disease.

The existence of bovine, human, avian, and vole types of tubercle bacilli, each of which has certain definite distinguishing characteristics, does not imply that any of these types are strictly host specific. If they were, the problem of preventing, suppressing, and eliminating the disease caused by each type of organism would be simplified. Instead, we are confronted with a disease of inconsistencies and one that is subject to remarkable variation. Tuberculosis is unique in its variable symptomatology, its unpredictable pathogenesis, and the inconsistent gross and microscopic tissue changes.

Especially important is the fact that each of the four types of tubercle bacilli is capable of infecting, even fatally, species of animals other than its natural host. This spectrum of pathogenicity is not only demonstrable by artificial experimental means, but is evidenced by natural transmission. Thus the mycobacterium of bovine tuberculosis is readily transmissible to man and to swine; the mycobacterium of human tuberculosis may affect bovine animals, swine, dogs, and monkeys. A striking analogous phenomenon is the pathogenicity of the organism of avian tuberculosis for several different species of mammals.

It is true that many mammals, including guinea pigs, dogs, cats, and human beings, are highly resistant to avian tubercle bacilli. Conversely, rabbits, swine, and mink are readily infected with these organisms. Usually bovine animals have considerable resistance to avian tubercle bacilli. When infection with this organism does occur in cattle, the disease is usually characterized by a circumscribed or localized focus of infection with little tendency to progress. A few exceptions to the essentially benign process have been noted and will be referred to subsequently.

Regarding the host-parasite relationship, there is evidence that in many instances infection of cattle and perhaps some other mammals with avian tubercle bacilli is limited to an intracellular parasitism. The tissue destruction and the usual structural changes that characterize tuberculous disease in animals that have greater susceptibility to the infectious agent do not ordinarily occur in cattle infected with avian tubercle bacilli.

Obviously, pathogenesis of this character and extent would be most difficult, if not impossible, to detect on gross examination and could be demonstrated microscopically only fortuitously. However, it is important to recognize that a mycobacterial infection limited in its extent to parasitism within the cytoplasm of a histocytic phagocyte may be capable of producing hypersensitivity to heterologous as well as to homologous tuberculins, and thus, it may provide a signal indicative of the presence of a potentially pathogenic mycobacterium.

The question of pathogenicity of avian tubercle bacilli for heterologous hosts and the relationship of avian tuberculosis to bovine tuberculosis eradication is indeed a complex problem and is by no means simple to clarify.

Abundant opportunities for natural exposure to avian tuberculous infection exist in certain areas of the United States. It follows, therefore, that some animals such as cattle, which are only slightly susceptible to avian tubercle bacilli, may become infected and develop minimal lesions and hypersensitivity to tuberculin.

From the results of many investigations over a period of several decades, the following facts pertaining to experimental infection of cattle with avian tubercle bacilli have been established:

1. Experimentally, cattle can be infected with avian tubercle bacilli.

2. The extent and severity of the disease depend on the age of the recipient, the route of inoculation, and the virulence of the microorganisms.

3. Cattle injected intravenously with virulent avian tubercle bacilli usually develop severe disease which is frequently lethal within four to six weeks.

4. Cattle inoculated subcutaneously tolerate the infective agent well in most instances. The subsequent disease is usually limited to the site of inoculation and to the regional lymph nodes. It may show, in addition, a slight tendency to disseminate to the abdominal and thoracic cavities.

5. Following the ingestion of avian tubercle bacilli by bovine animals, the mesenteric lymph nodes are usually involved and lesions may develop in the intestinal mucosa.

6. Widespread progressive tuberculosis does not occur in cattle infected experimentally with avian tubercle bacilli unless the infective agent is administered intravenously.

7. Experimental exposure of bovine animals to avian tubercle bacilli is followed by the development of hypersensitivity to avian tuberculin in most instances and to mammalian tuberculin occasionally.

Since the above summation indicates that cattle do have a limited susceptibility to avian tubercle bacilli, it is reasonable to expect that avian tuberculosis infections may occur in cattle under conditions of natural exposure. In a survey of published reports from 1893 to the present, over one hundred instances were found in which avian tubercle bacilli had been demonstrated in material from naturally infected bovine animals. Of the total cases reported, only about one-third have occurred in the United States.

It is quite unlikely that these instances of natural infection of cattle with avian tubercle bacilli are a true index of the actual situation. Supporting this point of view, a statement by Kelland, Frood, and Doyle, of England, who reported three cases of avian tuberculosis in calves, may be quoted: "In view of the considerable incidence of tuberculosis in poultry flocks on general farms in Great Britain, there would appear to be good grounds for believing that avian tuberculosis in cattle may be fairly prevalent."

The late Dr. L. Van Es stated in 1929 that "tuberculous infection of avian origin is by no means uncommon in cattle, . . . " Later Van Es and Martin studied the types of infection in 115 tuberculous cattle. They demonstrated mammalian tubercle bacilli in 100 of the cases. Avian tubercle bacilli were found in 11 of the remaining 15 cases. Most significant in this connection is the fact that of the 11 cattle in which avian tubercle bacilli were demonstrated, six had been sent to slaughter because of positive reactions to mammalian tuberculin.

In Europe, the foremost investigator of the natural infection of cattle by avian tubercle bacilli has been Plum of Copenhagen. As a result of extensive studies, Plum was able to show that cattle are susceptible to natural infection with avian tuberculosis and that in some instances abortion may be associated with intra-uterine infection with avian tubercle bacilli. Plum was certain that avian tubercle bacilli may sensitize cattle to both mammalian and avian tuberculins, with the homologous tuberculin inciting a more pronounced reaction than the heterologous product.

In America, the first reported case of cerebral and spinal meningeal avian tuberculosis in a bovine animal was reported in 1954 by Fincher and his associates. Tuberculous metritis was an additional item of interest in this case.

The data available do not provide adequate information concerning the probable incidence of avian tuberculous infection of cattle in America or in any other country. Among informed persons, there is little doubt that when cattle share the same premises with a tuberculosis-infected poultry flock, infection of a few to many of the cattle with avian tubercle bacilli is certain to occur. Furthermore, although these cattle may never have been exposed to either bovine or human tubercle bacilli, reciprocal hypersensitivity to mammalin tuberculin is likely to occur.

This hypersensitivity will persist as long as the tuberculous poultry flock is maintained and permitted to mingle with the cattle. Even though the cattle may be free of infection from either bovine or human tubercle bacilli, such reactors would routinely be destroyed on the basis of their positive reaction to tuberculin.

It is apropos at this point to recount briefly observations made many years ago by Schlotthauer and myself on a small dairy herd in Southeastern Minnesota in which avian tubercle bacilli were obtained on several occasions from necropsy material. The circumstances provide a lesson in epidemiology.

The animals were from a single herd from which, during the previous eleven-year period, twenty-one animals had been removed and slaughtered because they had reacted positively to tuberculin. At necropsy none of these twenty-one animals had revealed generalized or progressive lesions of tuberculosis. In a considerable number no grossly visible lesions were found. In the other reactors there were usually solitary localized subcutaneous tuberculoid lesions (so-called skin lesions), or indefinite changes of uncertain etiology in a few lymph nodes.

In the eleven cases studied various tissues were utilized for the making of cultures and, in most instances, for the inoculation of guinea-pigs and rabbits. In no instance was the bovine form of the tubercle bacillus demonstrated. However, four strains of avian tubercle bacilli were isolated from three of the animals.

From one animal, avian tubercle bacilli were secured from a tuberculoid lesion in the subcutis and from a mesenteric lymph node. From another animal the bacilli were obtained only from a mesenteric lymph node, and from the third animal the infective microorganism was isolated from an abscess in the subcutaneous tissue.

A survey of the premises on which the herd was kept disclosed that, since the herd had been established, a flock of approximately 100 chickens had been maintained on this farm. These chickens had had the freedom of the premises and had frequently fed in the barn and in the barnyard.

During our study, about half the birds in the flock were tested with tuberculin, and only one reactor was found. This hen had been on the

premises for 12 years. Necropsy revealed a nodular tuberculous mass in the wall of the cloaca, 4 cm. anterior to the vent. Numerous acid-fast bacilli were found in the necrotic portion of the lesion.

The evidence obtained in this study indicate that the source of the tubercle bacilli isolated from the cattle was the poultry flock. Since no instance of typical bovine tuberculosis had occurred in the herd for many years previously, it seemed logical to assume that some, at least, of the positive reactions to tuberculin were due to sensitization induced by avian tubercle bacilli.

A review of the information concerning the ability of avian tubercle bacilli to infect cattle and to sensitize bovine animals to tuberculin, suggests the following conclusions:

1. Under conditions of natural exposure, cattle have a limited susceptibility to virulent avian tubercle bacilli. When lesions occur, they are usually small, localized, and nonprogressive. Rarely, instances in which the disease was severe or generalized have been reported.

2. The lymph nodes of the alimentary canal are the sites of predilection for natural infection in cattle by avian tubercle bacilli.

3. Lymph nodes that appear grossly to be without morbid changes may, by suitable laboratory procedures, yield avian tubercle bacilli.

4. Following either natural or experimental exposure to avian tubercle bacilli, most cattle develop hypersensitivity to avian tuberculin. In cases of natural exposure this sensitivity is usually transitory, eventually disappearing if the animals are moved to a non-infected environment.

5. Frequently, probably in one third of the animals, cattle sensitized by avian tubercle bacilli under conditions of natural exposure respond positively to mammalian tuberculin. The reaction is usually of substandard dimensions.

6. In the United States, the avian tubercle bacillus sensitizes more cattle to mammalian tuberculin than is generally recognized.

Furthermore, at least some of the so-called "no-lesion reactors" react to mammalian tuberculin as a consequence of sensitivity induced by avian tubercle bacilli.

7. When tuberculosis of fowl is prevalent and it is reasonably certain that infection of cattle with bovine or with human tubercle bacilli has not occurred, infection with the avian tubercle bacillus should be considered as the source of sensitization to tuberculin. As a means of eliciting additional information concerning the tuberculin sensitivity,

reactors should be retested using simultaneously both mammalian and avian tuberculins. Experience indicates that the homologous tuberculin incites the more pronounced reaction.

In closing, I would like to return for a moment to what is implied by the title selected for me by the program committee. As you are aware, this reads: "Avian Tuberculosis and Its Relationship to Bovine Tuberculosis Eradication."

It is my opinion that there exists a significant relationship between tuberculosis of poultry and the prospects of eventually eradicating tuberculosis from cattle. To me, this relationship implies that unless tuberculosis of chickens and other farmyard fowl is eradicated, cattle will continue to be infected with tubercle bacilli, and some will continue to react to tuberculin. Consequently, valuable animals will be removed from the herd and needlessly slaughtered even though the last animal infected with bovine tuberculosis may have been detected and disposed of years previously.

I am aware that notable progress has been made in reducing the incidence of tuberculosis in poultry. I am aware, too, of the fact that a single tuberculous chicken with a single tuberculous ulceration anywhere along the intestinal tract may live for years. Such a tuberculous bird discharges continuously or intermittently with the fecal droppings enough virulent tubercle bacilli to infect, and sensitize to tuberculin, numerous cattle, swine, and other poultry.

It is obvious, at least to me, that tuberculosis, whether in man or in animals, will not and can not be eliminated by so-called "crash" attacks against the disease in any one species. The final objective must be the detection of all infected individuals whether they be animals or man. Persons with tuberculosis must be isolated during the active or contagious state of their disease. Animals found to be infected must be destroyed, and means must be employed to prevent the resurgence of the disease from obscure or hidden sources.

Much remains to be learned regarding tuberculosis of animals. Especially needed is additional information concerning the role of the avian tubercle bacillus in the sensitization of cattle to tuberculin. Furthermore, we should not ignore the possibility that certain unclassified mycobacteria may play a significant part in the development of heterologous hypersensitization.

The urgency of the problem should stimulate the desire to know, that there may accumulate useful information for the ultimate solution of the many complex questions. There is abundantly available raw material for investigation. With imagination, energy, persistence, and enthusiasm, he who would like to try, will find the quest exciting and rewarding.

PROMOTING THE ALL-PULLET FLOCK

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It is apparent that the eradication of tuberculosis must include the elimination of the avian type from poultry and swine, as has been mentioned several times already.

I was rather fortunate to work with Dr. C. D. Lee, the Extension Veterinarian, in the Department of Poultry Pathology in Iowa on a project that was begun in Iowa in 1947. This project was designed to determine how much avian tuberculosis there was in Iowa and also to see what we might do in the way of management by determining the practices already existing on the premises where infection was found.

One of the first things that was most apparent was that this is a disease that is still causing a very great loss. Great inroads have already been made toward eradication. Beginning in 1924, swine retained because of tuberculosis amounted to about 15 percent. In 1947 it was down to about 8.5 percent, and in 1956 down to a little over 3 percent. However, that still represents a large loss.

We notice it in Iowa because the poultry and swine industry are very important and are growing all the time, especially the poultry industry. The loss in the poultry industry, of course, is most noticeable as a result of loss in the condition of the birds, death loss, and loss in egg production. Almost 95 percent of swine infection, is contracted from poultry and the loss will, therefore, be reflected in swine wherever poultry infection is high.

It is quite apparent now, from the research we have on hand, that reduction of swine tuberculosis will be directly proportional to the decrease of tuberculosis in poultry. We are very fortunate to have such a situation with regard to controlling this disease in poultry and in swine, since it is easier to accomplish than perhaps the eradication of bovine tuberculosis. Neither poultry nor swine are usually kept on the farm for long periods of time, whereas dairy and beef cattle are kept much longer, thus giving the disease more time to develop visible lesions.

It is easier to finance and economically manage a turnover on a farm when it may be necessary to clean out tuberculosis in swine and poultry because of the difference in costs, and the fact that in most instances, in Iowa at least, the poultry industry is somewhat of a sideline quite often managed by the housewife and so does not represent such an investment that a change in management practices will completely upset the farm operations or make new mortgages necessary.

This survey was carried forward cooperatively with the Iowa Department of Agriculture, the Agricultural Extension Service, Iowa State College, local veterinarians, hatcherymen, produce dealers, the Iowa Poultry Improvement Association and the Iowa Swine Producers Association. We feel that the fact that it was a cooperative project did much toward helping us to get the information that we wanted.

Before I forget, I would like to mention that in one county in which this work was carried forward practically half of the arrangements for the survey were made by a local practicing veterinarian. His enthusiasm and willingness to help was something that Dr. Lee and I will always remember.

One of the fortunate things about avian tuberculosis control and eradication is that it is rather easily diagnosed in the field. Veterinarians and people interested in poultry husbandry often miss the opportunity to observe poultry and make recommendations. I'm sure this is one of the things that could be done more often and more thoroughly. From my own experience I have found that people are happy to get help.

Many times they show their appreciation to you later by telling you of the results they get. And results are often rapid because one of the things about poultry is that they respond quite rapidly to good management practices. Anything that you can give in the way of disease control and nutritional advice while on a farm is certainly worthwhile.

We should first consider the attitude of a chicken with tuberculosis. The wattles and comb are pale, there is fading out in the beak and shanks, and you will notice by observing the birds that they do not show much activity, and their appetites are considerably retarded.

If you pick these birds up, and quite often in a badly infected flock they are very easy to pick up, you will find that they do not weigh very much. By palpating the breast area you will notice that there is considerable loss of flesh on the breast muscles. That makes it rather easy to determine if it is a good idea for you to perform further examination of such a specimen. I've done it many times and I know that we have many veterinarians who do it routinely. If Dr. Lee were here I think one of the things that he would tell you is that it hasn't been too many years ago that at veterinary meetings and demonstrations, when speakers and people, who had something to say about poultry, got up you saw quite an exit out the back way. Many veterinarians were not interested in poultry.

Due to the economic importance now, that interest has reversed itself and veterinarians are showing a great deal of interest and assisting very much in the eradication of poultry diseases.

Let us now consider the pathology found in infected birds. Tuberculous nodules on the liver and spleen are commonly found among infected birds on autopsy. Sometimes the liver will be enlarged and sometimes the lesions will be barely visible to the naked eye, but typical lesions are found in most infected flocks.

I should mention here that the procedure for examining these birds on the farm should be one that is carefully handled. The autopsy should be done neatly, using rubber gloves, and should be performed in a businesslike manner. I believe that everyone from the producer to the housewife who might be observing you appreciates the procedure that you use when handling diseased birds.

Now let us consider a tabulation we have made from our survey. The first tabulation is of mixed flocks, (pullets and hens), housed together, a total of 251 flocks. These birds -- a total of 58,182 -- were individually tuberculin tested. The number of positives was 3,282 and the percent positives was 5.64. The number of flocks positive amounted to 159, and the percentage of flocks positive, 63.34. I think you should keep in mind that these were mixed flocks composed of pullets and hens housed together.

Another tabulation made covers all pullet flocks, or birds sold each year at the end of production. This, incidentally, is something that we hope to achieve on a more universal scale. In this particular case, there were 169 flocks composed of 33,769 birds. Of these birds, only 84, or 0.24 percent showed a positive test. At the same time, only 22 flocks, or 13.01 percent were positive.

The next group we studied consisted of 48 old hen flocks in which all of the birds were kept two years or longer. Thirty of these flocks, or 62.50 percent, showed positive reactions, while of a total of 5,382 birds, 620 gave a positive test. This amounted to 11.51 percent of all birds tested. The increase in incidence among old hens is of significance when you visit these premises and see what is going on.

The next group of figures represents the total of all birds, both old hen and mixed flocks, and all pullet flocks. Involved were 468 flocks containing 97,323 birds. When these birds were tuberculin tested, we found 3,926 or 4.03 percent, showed a positive reaction. When we broke the figures down on a flock basis 211, or 45.08 percent, showed infection.

To provide further background on these tests, we then did a study of the mixed flocks in which both old hens and pullets were housed together. This was somewhat different than previous surveys, since the tests had to be made on the spot by the inspectors

because we had to record at the time the observations were made whether the reactors were old hens or pullets.

In this case we studied a total of 153 flocks containing 25,282 pullets and 13,110 old hens. Of these totals, we found that 93, or 0.36 percent of the pullets showed a positive reaction and 2,462, or 18.77 percent of the old hens reacted to the tests. You will note that even though the pullets and old hens were housed together, the pullets still showed a low incidence of disease. On the other hand, I do not mean to imply that they are not susceptible, because they certainly are.

When we found positive reactors in poultry on farms where hogs were present, except for market hogs, of course, we tested those hogs. Here we used both mammalian and avian tuberculin on the hogs and we had practically no reactors as far as mammalian tuberculin is concerned. Since we have such a heavy hog population, that is not surprising since on many farms we found the poultry roosting and foraging on the same grounds with the hogs.

It is easy to see why the mammalian type of tuberculin did not seem too important in hogs in this survey. For example, we studied a total of 2,660 hogs in 103 herds. And while 22 percent of the herds were infected, they only contained a total of 87 reactors, or 3.27 percent of all hogs checked.

It is quite evident that the old birds are the offenders and spreaders. The survey certainly would indicate this and the experience of observing some of these flocks over a period of time has borne this out. Many of these old birds completely recover insofar as appearance is concerned but they are carriers and spreaders to the young birds, and that is one of the hazards of keeping them in the flock.

Since the incidence in pullets is about 0.07 percent and in the old hens 10.5 percent, it would appear that we should do everything that we can to encourage the so-called all-pullet flock. We have been very successful in getting many Iowa producers to adopt that method of poultry production.

Following this are a couple of pointers that I think you will find of value when you talk to people about this: Pullets will lay 20 to 30 percent more eggs annually than old hens, and will lay 20 to 30 percent more eggs in their first production year than in their second. This is an economic factor in our favor in talking up the all-pullet flock.

It will take almost the same amount of feed to feed a hen through the moulting period as to raise a pullet to production,

another good argument. In fact, there is no argument about it, since it's an economically sound reason why we should encourage the all-pullet flock. Most important, it will stop the transmission of the avian type of tuberculosis to swine, since that is where they receive over 95 percent of it.

A few other things that might be valuable in management of the flock, are thorough cleaning of the laying houses and all other buildings and equipment with a hot lye solution, one can of lye to about 15 gallons of water. That is mainly to dissolve some of the debris and to assist with the cleaning. Next step would be to disinfect the premises with an approved cresolic acid solution, and we try to get them to do that shortly before putting the pullets in the laying house. If a movable house, we also recommend spraying the base of the house with a preparation such as black leaf forty, crankcase oil, carbolinium, or some other similar preparation. I should add that this type of management practice as far as poultry is concerned will also eliminate great numbers of other infectious diseases and parasites of poultry.

House the pullets in the fall and keep them housed until sold. Housing will, of course, keep them away from swine, and housing of the laying flock now is almost standard practice. Where forage space is used, rotate the yards and lots for both hogs and birds, cultivate and seed when necessary, and always raise the chicks on clean lots and shelter away from any old used lots or old buildings.

If you have birds that are suspected of having tuberculosis they should be burned rather than thrown over the fence for the hogs to feed on, which used to be a very common practice, and unfortunately still is in some areas. The value of the protein does not offset the danger involved to the hogs.

Culling of the birds is, of course, a continuous process that should never stop. It can be almost a daily practice and I'm sure that every poultryman who is in business very long would agree that culling is one of the things that he must never neglect.

In conclusion, I might add a couple of more benefits to be derived from the all-pullet flock. Those benefits are: Better profit in poultry and eggs; elimination of the avian type of tuberculosis, largely from swine; reduction of other diseases and parasites by the same process of management; and last but not least, cattle will not be sensitized to the avian type of tuberculosis. I believe that if we diligently practice and advocate these methods of management we will have taken another giant step toward the eradication of tuberculosis.

TABLE 1.--Mixed Flocks: Pullets and hens housed together

County	No. Flocks	No. Birds	No. Positive	Percent Positive	No. Flocks Positive	No. Flocks Positive
Hamilton........................	27	5792	190	3.28	18	66.66
Buena Vista.....................	31	7512	286	3.80	25	80.64
Cerro Gordo.....................	16	2863	148	5.16	7	43.75
Lucas...........................	24	4283	79	1.84	8	33.33
Winneshiek......................	32	8707	1054	12.10	27	84.37
Henry...........................	24	5113	126	2.46	13	54.16
Page............................	17	4123	42	1.01	8	47.05
Ida.............................	21	4032	400	9.92	15	71.42
Clinton.........................	12	2648	269	10.15	9	75.00
Wright..........................	22	6205	346	5.57	13	59.09
Benton..........................	5	1476	36	2.43	2	40.00
Allamakee.......................	8	1821	176	9.66	6	75.00
Shelby..........................	12	3607	130	3.60	8	66.66
Total........................	251	58182	3282	5.64	159	63.34

TABLE 2.--All Pullet Flocks: Birds sold each year at end of production

County	No. Flocks	No. Birds	No. Positive	Percent Positive	No. Flocks Positive	No. Flocks Positive
Hamilton........................	23	3801	5	.13	4	17.39
Buena Vista.....................	25	4666	51	1.09	6	24.00
Cerro Gordo.....................	14	2837	3	.10	2	14.28
Lucas...........................	6	1094	0	.00	0	00.00
Winneshiek......................	8	2147	10	.46	2	25.00
Henry...........................	16	3751	2	.05	1	6.25
Page............................	13	2165	1	.04	1	7.69
Ida.............................	10	1714	0	.00	0	00.00
Clinton.........................	10	1602	3	.18	1	10.00
Wright..........................	27	6387	4	.06	2	7.40
Benton..........................	10	2295	5	.21	3	30.00
Allamakee.......................	0	0	0	0	0	0
Shelby..........................	7	1310	0	0	0	0
Total...........................	169	33769	84	.24	22	13.01

TABLE 3.--Old Hen Flocks: Birds kept over 2 years or longer

County	No. Flocks	No. Birds	No. Positive	Percent Positive	No. Flocks Positive	Percent Flocks Positive
Ida	12	1296	219	16.89	11	91.66
Clinton	8	669	74	11.06	3	37.50
Wright	20	2218	143	6.44	10	50.00
Benton	1	125	1	.80	1	100.00
Allamakee	7	1074	183	17.03	5	71.42
Shelby	0	0	0	0	0	0
Total	48	5382	620	11.51	30	62.50

TABLE 4.--All Birds

County	No. Flocks	No. Birds	No. Positive	Percent Positive	No. Flocks Positive	Percent Flocks Positive
Ida	43	7042	619	8.79	27	62.79
Hamilton	50	9583	195	2.03	22	44.00
Buena Vista	56	12178	337	2.76	31	55.35
Cerro Gordo	30	5700	151	2.64	9	30.00
Lucas	30	5377	79	1.46	8	26.66
Winneshiek	40	10854	1064	9.80	29	72.50
Henry	40	8864	128	1.44	14	35.00
Page	30	6288	43	0.68	9	30.00
Clinton	30	4919	346	7.03	13	43.33
Wright	69	14810	493	3.32	25	36.23
Benton	16	3896	42	1.07	6	37.50
Allamakee	15	2895	359	12.40	10	66.66
Shelby	19	4917	130	2.64	8	42.10
Total	468	97323	3926	4.03	211	45.08

TABLE 5.--Breakdown of Mixed Flocks

County	No. Flocks	No. Pullets	No. Pullets Positive	Percent Pullets Positive	No. Old Birds	No. Positive Old Birds	Percent Positive Old Birds
Winneshiek..........	32	5238	6	.11	3469	1022	29.46
Henry...............	24	3399	4	.117	1714	122	7.11
Page................	17	2785	1	.03	1338	42	3.13
Ida.................	21	2549	19	.74	1483	381	25.69
Clinton.............	12	2549	19	.74	759	250	32.93
Wright..............	22	4145	13	.31	2060	334	16.21
Benton..............	5	1039	4	.38	437	32	7.32
Allamakee...........	8	1267	19	1.49	554	157	28.33
Shelby..............	12	2311	8	.34	1296	122	9.41
Total..........	153	25282	93	.36	13110	2462	18.77

TABLE 6.--Hogs

County	No. Herds	No. Hogs	No. Reactors	Percent Reactors	Percent Herds Infected
Ida....................................	5	110	6	5.45	19.3
Clinton................................	9	170	23	13.52	33.33
Wright.................................	52	1640	36	2.19	16.42
Benton.................................	11	224	7	3.12	18.80
Allamakee..............................	13	195	13	6.66	5.38
Shelby.................................	13	321	2	.62	15.38
Total..............................	103	2660	87	3.27	22.00

POST MORTEM TECHNIQUE AS APPLIED TO TUBERCULOSIS REACTORS

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Post mortem is accomplished primarily by cutting of tissues, by palpation, and by visual observation. By performing this inspection in a scheduled sequence the veterinarian has in mind his principal objective--to allow only that meat which is wholesome to be passed for human food.

Post mortem inspection of a tuberculosis reactor is divided into four general steps; cervical, viscera, rail, and final.

Cervical inspection includes incision of the atlantal, mandibular, suprapharyngeal, and parotid lymph glands. In addition, the tonsils and muscles of mastication are incised, and the tongue examined. At this time it is necessary to ensure identity of the carcass and the parts derived from it. To accomplish this, a sectioned "U. S. Retain" tag is attached to the carcass as well as the parts. The metal reactor ear tag provides additional individual animal identification.

Viscera inspection involves cutting the right and left bronchial, medial and posterior mediastinal, and portal lymph glands. The heart is incised to expose all chambers as well as opening of the trachea to observe the inner surface.

The spleen and mammary organ are sliced repeatedly to expose the interior surfaces. The lungs and liver are palpated to detect any tuberculosis lesions not visible by surface observation. The mesenteric glands are incised and the digestive viscera observed for any evidence of tuberculosis lesions.

At any time during any stage of inspection additional examination is made if the inspector deems it necessary.

The hide, when removed from the carcass, is placed so that a complete survey can be made to detect any skin lesions which may be present.

Rail inspection includes observation of all surfaces of the carcass previously not accessible, and incision of the precrural, superficial inguinal, internal iliac, lumbar, and renal lymph glands as well as examination of the kidney, adrenal, pleura, and peritoneum.

Final inspection includes exposing and incising of body lymph glands, such as popliteal and prescapular when indicated, and the evaluation of the extent, location, and type of tuberculosis lesions which have been found in all the previous stages of inspection.

The Federal Meat Inspection Regulations classify the degrees of tuberculosis which may be found and specify the disposition that is required in each case. Parts containing tuberculosis lesions are condemned, but generalized tuberculosis requires condemnation of the carcass. Slight lesions which are encapsulated, if properly removed, may permit the part to be passed for food. Cases which would appear between these extremes are passed for cooking.

Special reports showing the results of the inspection are prepared for the Animal Disease Eradication Division.

In summary, a tuberculosis reactor receives cervical, viscera, rail, and final inspection. In addition to the metal reactor tag, the carcass is completely identified with a "U. S. Retain" tag and is disposed of as "passed for food," "passed for cooking," or "condemned" in accordance with recognized food hygiene standards.

PRACTICAL APPLICATION OF CLEANING AND DISINFECTION

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We realize that many times an ideal job of disinfection cannot be obtained on all premises; however, we as regulatory veterinarians and practitioners should always strive for an effective job.

From a bacteriologist's viewpoint, actual decontamination of premises would seem impossible. Therefore, effective disinfection must depend largely upon cleaning, washing, or diluting the contaminant so that pathogenic doses are not available to the remaining animals in the herd. Too many laymen are of the opinion that chemical disinfectants are all-powerful. From a practical viewpoint, the cleaning and washing must be emphasized constantly.

Unfortunately, some members of the veterinary profession have adopted the attitude of the pure bacteriologist. They argue that the disinfecting of boots and equipment is not effective because the materials are not in contact with the chemicals for an effective length of time. It is evident, in some cases, that we must stress cleaning, washing, and disinfection to some of our profession.

Practicing and regulatory veterinarians engaged in eradicating animal disease should, in the first place, use precautionary measures in their work. The first thing of importance is that the veterinarian be equipped to do a thorough job. He must protect himself and his clients to prevent any spread of disease. He should be equipped with footwear and other protective clothing, and all equipment used in handling animals

should be scrubbed with a stiff brush, using a disinfectant, before he leaves the herd owner's premises. If a cattle chute was used on the premises, it should be thoroughly cleaned by sweeping with a stiff, thick brush or broom. And after a thorough cleaning, a disinfectant of the veterinarian's choice should be used.

Cleaning and disinfection is done in public stock yards and specifically approved sales barns under the supervision of Federal, State, or practicing veterinarians. Quarantine pens in these establishments are provided so that diseased animals can be controlled. All public stockyards and specifically approved barns have adequate cleaning and disinfectant equipment set up by the management to provide protective service for truckers and livestock owners.

We as veterinarians should instruct the herd owner, after diseased animals are properly identified, to see that the proper form accompanies the animals and that the trucker or owner who transports the diseased animals properly notifies the personnel who receives them, whether yard company, personnel at Federally inspected plant, or specifically approved barn, to make sure that these people note these animals are diseased and should be handled as such.

In my experience in various stock yards, time and time again animals came in not properly identified, or the owner or trucker did not identify the animals at the time they arrived at the yards. Often they were overlooked by stock yard personnel because the brand would not be legible, or not properly seen, and as a result considerable embarrassment would be caused to State and Federal personnel in the yards since the reactors would be yarded outside of the quarantined area with non-reactor animals which have gone back to the farm.

When cases of this nature occurred, the pen involved would have to be cleaned and disinfected, a step which could have been avoided if the animal had been properly identified.

One of the better leaflets which we have received on cleaning and disinfection is, "Clean, Wash, and Disinfect Livestock Carriers to Prevent the Spread of Diseases." This bulletin published by Livestock Conservation, Inc., has been used in stockyards, and at the present time we have these bulletins distributed in various sale barns throughout the State.

This leaflet contains information on why cleaning, washing, and disinfecting are done (including picture illustrations); directions in table form to make spray solutions for different diseases; and types of sprayers for every job.

Public stockyards are set up for cleaning and disinfecting trucks and the premises. They have mobile units at some yards which can be moved from place to place for an annual cleaning and disinfecting of certain portions.

Facilities are set up by either stockyard management or properly supervised private operators for the disinfection of the vehicles arriving at the market. Disinfection during regular hours is supervised by State or Federal employees in the course of their other duties and a responsible market official is delegated to supervise the operation during other hours.

In the area of equipment, pressure sprayers should be available which develop 150 pounds of pressure per square inch. Spray nozzles should be provided which will both thoroughly wet and penetrate cracks and crevasses. If an orchard type nozzle is to be used, a No. 5 whirl plate opening will effectively accomplish this. Smaller openings frequently result in a greater portion of the disinfectant being suspended in the air and less on the surface to be treated.

In approved livestock markets, we have found that the use of a foot box, approximately $1\frac{1}{2}$ to 2 feet square, and 6 inches deep, placed at the side of the entrance and exit of the barn, is very well received by all concerned. This box is filled with sawdust or sponge rubber containing a solution of 2 to 3 percent cresylic disinfectant or 4 percent soda ash. The sale barn is cleaned and disinfected weekly and the box is easily cleaned at the same time. In our observations at the various barns, when people enter or leave the sale area over 95 percent step into the box of disinfectant.

Around the arena of sale barns, operators have been using a rubber base floor and deck enamel. This can be washed with water under pressure with the result that manure is readily flushed off. This results in a much more practical cleaning and leaves a better appearance than when whitewash or other type paints are used.

When infectious diseases occur on farms, we then have a problem of cleaning and disinfecting to prevent the continuation of the spread of the disease from a contaminated environment. In animal disease eradication, this step should occur immediately after removal of known infected animals. I am sure we will all admit that our procedures for various diseases have not always been uniform, and on some occasions may not have been carried out as thoroughly as we would like. Farm cleaning and disinfection is an important part of all disease eradication programs.

In dealing with exotic diseases, such as foot and mouth disease, herds in their entirety are destroyed and buried on the premises. Regulatory personnel then carry out cleaning and disinfection procedures. In dealing with diseases under eradication programs, such as tuberculosis and brucellosis, diseased animals are removed from the farm as promptly as possible and the remainder of the herd continues to use the premises.

In protecting the remainder of such herds, it is important that we clean and disinfect as promptly and thoroughly as possible. The necessity for early cleaning and disinfecting has been recognized in our

indemnity regulations. Our efforts, therefore, need to be directed toward accomplishing that objective in the best practicable manner. In the past we have depended to a large extent upon the owner to perform the cleaning with varying degrees of supervision.

In order to assure prompt cleaning, it is essential that the owner be given instructions as to what should be done and why, in order that he may arrange to start his cleaning immediately after removal of the animals. It is preferable that this be done through verbal instructions from the veterinarian or regulatory official who identifies the infected animals. The veterinarian should also be provided with written instructions to leave with the owner in addition to his verbal instructions. These should include information on management practices as well as actual physical cleaning.

In herds where there has been evidence of spread of infection as represented when more than one tuberculosis case is found, or where active progressive brucellosis infection exists, we believe that direct supervision of the disinfection and inspection of the preliminary cleaning is indicated.

Unless power spray equipment is available on the farm, the person supervising the disinfection should have equipment available. This can be provided by a gasoline driven power sprayer mounted on a suitable truck. Special attention should be given to be sure that water troughs and drinking cups are not overlooked.

In many other herds under the circumstances existing at this time, it will be necessary to depend on herd owners to carry through with disinfection. We must be sure that the owner has in his possession complete instructions as to the disinfectant to be used and the method of its application. In addition we mail a statement from our central office containing the essential steps necessary on the part of the herd owner to bring about disease eradication. Included in this statement is a reminder of the need for early cleaning and disinfection if it has not already been done.

We have distributed a form prepared for use in the certification of disinfection which includes a check list on the reverse side.

Part one covers infected herd and premises data to be completed by the testing veterinarian. Information to be completed includes: owner's name, address, and county; name of the testing veterinarian, disease for which tested, date of test, results of test, reactor tag numbers, and parts of the premises occupied by the herd.

Section "B" states the existing official regulations which point out that proper cleaning and disinfection should be in accordance with the requirements and recommendations of the appropriate State and Federal officials.

Section "C" is the statement of the owner to be completed following disinfection of the premises, stating the date reactors were shipped to slaughter, name and address of the commission firm or slaughtering establishment receiving the reactors, amount and kind of disinfectant used, date disinfection was completed. This statement must be signed by the owner or manager and the date of signing indicated.

Notation at the bottom of the form instructs that the forms, when completed and signed, should be mailed to the office of the veterinarian in charge. It also contains a statement that indemnity claims, if involved, may not be approved for payment until the certificate is dated, signed, and received at that office.

Part two on the reverse of the form is a cleaning and disinfection check list. If cleaning and disinfection is not required on the premises, the first block opposite "A" is checked, and an explanation of the circumstances given in the space provided at the bottom of the sheet.

If cleaning and disinfection is required on the premises, the block opposite "B" should be checked, and the testing veterinarian or regulatory personnel should review the items under "Cleaning, Management, and Disinfection," with the herd owner, checking those items applicable to the particular premises.

The following items are listed under "Cleaning."

(a) Watering troughs, all mangers, feed racks or boxes, tanks, or cups, to be cleaned thoroughly before being scrubbed with a lye solution. (1 lb. concentrated lye to 6 gals. water) (Note precautions on label). Carefully rinse with clear water before using.

(b) Ceilings, walls, partitions, posts, etc., to be swept free of cobwebs and dirt.

(c) Remove all dried accumulation of bedding, manure, and other material from floors, walls, partitions, posts, stanchions, etc., by scraping. They should then be scrubbed with same strength lye solution, using a stiff broom or brush.

(d) All feed room and cleaning equipment should be thoroughly cleaned and scrubbed in the lye solution.

(e) All manure, litter, and other refuse, from building, yards, etc., should be removed to a place inacessible to livestock.

(f) The upper surface of all earthen floors should be removed and replaced, if desired, by uncontaminated soil.

(g) All earthen floors should be thoroughly limed after attention as above.

(h) Accumulation of manure around feed bunks and water troughs should be removed.

Under "Management," are listed:

(a) Maternity stalls recommended.

(b) Drainage from buildings, yards, corrals, etc., to be diverted from cattle areas or fenced as detailed.

(c) Water pools, swampy areas, and ponds to be drained or fenced as detailed.

(d) Water to be checked for possible contamination.

(e) Poultry and other fowl to be confined away from cattle.

(f) Light supply in buildings should be adequate.

(g) Ventilation satisfactory.

Disinfection items are:

(a) Obtain approved disinfectant ONLY, and provide the following data:

Disinfectant:
Manufactured by:
Amount Purchased:
Purchased from:

(b) Apply liberally to all cleaned surfaces with spray (Preferably power equipment) in the ratio of one gallon disinfectant to each thirty gallons water.

This cleaning and disinfection check list is to be completed in duplicate, dated and signed by the testing veterinarian or regulatory personnel, the original left with the owner to be mailed, as directed, when cleaning and disinfection is completed and the certificate signed. The copy will accompany the indemnity claim papers forwarded to the central office.

In conclusion, I hope that I have clearly presented my views on the practical application of cleaning and disinfection in various animal concentration points where disease is more readily spread. Every problem has a solution. I believe the greatest obstacle to proper cleaning and disinfection of infected premises is that the farmer does not fully appreciate the necessity for the work. By using the check list form he will better understand what is required to do a thorough job of cleaning and disinfecting after removal of reactors.

MECHANISMS OF INFECTION AND RESISTANCE

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It is obvious that infection is the work of two factors - the invasive and infectious characteristics of the microorganism and the susceptibility of the host. The variable qualities of both of these factors are responsible for the variables of disease. The elaboration of these variables one finds in textbooks of microbiology and pathology.

In discussing this subject, one is immediately confronted with the problem of which comes first. Obviously both factors operate simultaneously in the process of infection. Consequently, the best method for presenting the subject is to outline a few basic facts concerning the infectious agent and then some facts concerning the resistance of the host.

In considering the infectious agent, a number of properties come to mind. The first is size. With the exception of the filterable viruses, one finds little influence of size in terms of infectivity. However, even among agents which are classified as bacteria, one may see variabilities in the quality of invasion.

For example, the leptospira are well known for their invasive properties, and it is said that one merely needs to contaminate the unbroken skin with these organisms and infection may result. It is quite likely that this may be due to the shape and elasticity of the organism rather than size itself.

It is obvious that a filterable virus as small as that of foot and mouth disease may penetrate into and between epithelial cells much more easily than can an organism the size of _Bacillus anthracis_.

The ability of organisms to produce infection apparently lies in the physiology of the organism. This quality to produce disease is more generally discussed under the term of "virulence".

The characteristics which make one organism a harmless saprophyte and another a deadly pathogen are not thoroughly understood. Infectious disease is, no doubt, primarily a result of the action of certain chemical components of the organism along with the reaction to this chemical on the part of the tissues of the host. Whether disease is a result, therefore, of the potency of the organism or the weakness of the host is difficult to determine.

There is a tendency to refer to the causal microorganism as the inciter of disease and to the host merely as a susceptible recipient. Bacteria vary in their ability to cause disease. This ability is usually

summed up in the use of the terms "virulence" or "pathogenicity". For that reason, an organism is referred to as avirulent, slightly virulent, very virulent, or extremely virulent. The use of such modifying terms for various species of bacteria is based upon factors emphasized in the following discussion.

Some species of bacteria are able to produce toxins which are more lethal than those of other bacteria. This is true also in some strains of the same species.

A good example of a toxin-producing organism is the bacillus responsible for tetanus in man and animals. This organism may be classified as a saprophyte but the effects of its deadly toxin make it apparent that it should be called a pathogen.

Washed spores of this organism may be given orally to animals without producing injury. In fact, they may be introduced into healthy tissue without causing symptoms of the disease. However, if such spores are introduced into tissues along with necrotic tissue, or with chemicals which may kill tissue cells, they germinate and produce a toxin which is disseminated throughout the body causing the muscle contraction characteristic of the disease.

If the organism is grown artificially so that toxin is produced, minute amounts of it, entirely free of the bacilli, will cause the same typical symptoms.

An example of an entirely different type of organism is Bacillus anthracis, the cause of anthrax. This is a sporeforming bacillus. When washed spores are placed in healthy tissues, they germinate, the resulting organisms multiply rapidly and spread throughout the body of the animal quickly producing death.

When this organism is grown in artificial media, the cell-free filtrate will not produce symptoms of the disease. These two examples represent the two extremes of pathogenic activity, with many species of bacteria being both toxic and invasive.

In addition to toxin, mentioned above, there are other substances produced by bacteria which endow them with virulence. Some of these substances are toxins while others are extracellular enzymes.

The production of hemolysin by bacteria has long been associated with virulence. While this may be true of some species it is not true of others, because entirely nonpathogenic species produce hemolysis.

Recent studies on hemolysin (Bernheimer, 1947) indicate that this material is enzymatic. The substrates in which these enzymes reside are known. Quite likely the substrates act as antigens explaining why hemolysins have been classified as toxins.

A single bacterial species may produce more than one hemolysin. The Group "A" hemolytic streptococci, for example, produce two hemolysins which differ in their chemical properties and the method by which they cause hemolysis of erythrocytes. These hemolysins have been designated streptolysin "O" and streptolysin "S". Streptolysin "O" is a rather labile protein containing sulfur and is oxidized by atmospheric oxygen. It can be reactivated by such a reducing agent as sodium hydrosulfite.

This type of hemolysin is produced by many different species of bacteria. It is neutralized by specific immune serum and by cholestrol. The antisera from an animal immunized by one of the "O" hemolysins will neutralize the others, hence it appears that they are not specific.

Streptolysin "S" is a lipoprotein and is not neutralized by cholesterol and is not reversely oxidizable. Antiserum for this hemolysin is prepared with difficulty and it does not neutralize streptolysin "O" It is extractable from the streptococcal cells by means of serum - the "S" means serum extractable -- and is very unstable, being preserved only by lyophilization.

This hemolysin produces degenerative effects on heart muscle and other parenchymatous organs as well as hemolysis. There is little doubt that it is associated with virulence. Hemolysis noted on the blood agar plate is considered due to streptolysin "S". However, this does not mean that "O" has not been produced. It may have been oxidized.

Blood of horses has been shown to possess antistreptolysin "O" which prevents the elaboration of this substance. The blood of all animals has not been assayed for the presence of antihemolysin, but rabbit blood is known to be comparatively free of it, consequently is most suitable for the preparation of blood agar.

Many different species, particularly the staphylococci, produce leucocidin which is able to cause the destruction of leucocytes. It appears likely that this material is identical to hemolysin "O", inasmuch as it is oxidized in the same reverse manner.

The accumulation of leucocytes in suppurative processes, and the destruction of those leucocytes which have phagocytized masses of bacteria, makes it evident that the substance leucocidin is a protective mechanism which enables bacteria to multiply more abundantly in infected tissue.

The description of "fibrinolysin" by Tillett and Garner in 1933 contributed another substance by which certain of the streptococci and staphylococci may be enhanced in virulence. This substance, now called streptokinase, causes the dissolution of fibrin clots in a few minutes. It is known to be a kinase which activates a proteolytic enzyme normally present in plasma in an inactive form.

The absence of fibrin is one of the characteristics of certain acute types of a streptococcal infections, so it is presumed that this is due to streptokinase. This is supported by the fact that when the specific antibody, antistreptokinase, appears in the blood stream, fibrin appears in the infected tissues.

Pathogenic strains of <u>Micrococcus</u> <u>aureus</u> produce an enzyme-like substance, called coagulase, which is able to cause the coagulation of blood plasma from rabbits and human beings. The role this substance plays in virulence is not known. However, since most staphylococcic infections are localized, it may be presumed that the formation of coagulated masses of plasma about colonies of the organism in tissue, prevents the penetration of leucocytes and lytic agents of the body defense mechanism.

<u>Clost</u>. <u>perfringens</u>, as well as other members of the gangrene group of Clostridia, produces toxins which have a marked effect upon the blood-vascular system. It has been shown that this toxin is a lecithinase which brings about the hydrolysis of lecithin when acted upon by calcium ions. Lecithinase causes marked hemolysis and necrosis of other cells, so it is apparent that it has a direct influence on disease produced by these organisms.

Culture filtrates of <u>Clost</u>. <u>perfringens</u> also contain another proteolytic enzyme which has been called collagenase. This substance causes the disintegration of muscle tissue of laboratory animals by decomposing the reticular scaffolding.

It has been suggested by MacFarlane and MacLennon, 1945, that collagenase may be responsible for the pulpy condition of muscle found in cases of gas gangrene. Both lecithinase and collagenase are neutralized by the action of commercial antitoxin.

Hyaluronic acid is a viscous, polysaccharide acid of high molecular weight, present in the intercellular ground substance of many different tissues. Numerous bacteria produce the enzyme hyaluronidase which hydrolyzes hyaluronic acid. Duran-Renals, 1942, found that the injection of this enzyme into tissues increased permeability and allowed the rapid spread of injected solutions, India ink, and bacteria. He referred to the substance as a spreading factor.

Previous to 1945 this investigator has observed the presence of this material in aqueous extracts of rabbit, guinea pig, and rat testes. It has since been shown that numerous bacteria, staphylococci, streptococci, pneumococci, corynebacteria, and colstridia produce hyaluronidase. The invasive qualities of these bacteria reenhanced, no doubt, by this substance which enables the bacteria to penetrate through the barrier of endothelial and epithelial cells.

It must be kept in mind, when considering the relationship of the toxins and enzymes to virulence, that all of these substances are not produced by all bacteria. One substance may be of aid to one species and another substance to another species. In general, the bacteria producing disease in animals have not been sufficiently investigated to know the virulence pattern of all of them.

Bacteria in general may lose their virulence when subjected to certain environmental conditions such as growth on ordinary artificial media, at high temperatures, and in contact with chemicals. This decrease in virulence is known as attenuation.

The anthrax bacillus maintains its virulence when grown on ordinary media but loses it when grown at 42° C. The virulence of bacteria can be increased also. The less virulent strains of hemorrhagic septicemia bacteria can be increased by successive passages through mice and egg embryos.

Certain avirulent strains of bacteria can be made fully virulent when grown on media containing blood or blood serum. The loss, as well as the acquisition, of virulence appears to be involved in the phenomenon of dissociation. Bacteria in the "S" stage are more fully virulent than those in the "R". Capsulated bacteria are more virulent when the capsule is present than in the dissociative noncapsulated state.

Organisms are more virulent when they contain as a part of their chemical structure a specific polysaccharide, a substance which also has an important role in immunity. The Gram-negative bacteria possess an endotoxic substance known as "O", or somatic, antigen, which is composed of carbohydrate, protein, and phospholipid. This component is located at or near the cell surface and is liberated upon the lysis of the cell. It is known to be highly toxic, but not in the manner of the various toxins and enzymes produced by Gram-positive cocci and bacilli.

Injections of small amounts of purified endotoxin will produce a sharp rise in temperature, increase in blood sugar, and decrease in organic blood phosphorus in experimental animals. The pyrogenic substances present in water are believed to be endotoxic material resulting from the autolysis of Gram-negative bacteria present in the water. For this reason solutions used for intravenous injections should be made of freshly distilled water.

The number of bacteria present in the initial invasion of a host undoubtedly is a factor in virulence. The apparent increase in the virulence of a microorganism causing an infection in a herd is partially due to the increase in the number of bacteria to which the susceptible animals have access. It is obvious that two infected animals would liberate more bacteria than one, four more than two, etc.

The specificity of one species of bacteria for certain tissue has a marked bearing upon the determination of the virulence of that species. In other words, the degree of virulence can be determined somewhat by the type of tissue affected. It is obvious that a microorganism which produces a rapid and fatal pneumonia is more virulent than one which attacks intestinal tissue. One organ, in this instance, is more vital than the other, and its destruction causes the death of the host more quickly.

The extent to which bacteria are able to multiply in tissue also has some bearing upon virulence and is governed greatly by the response of the defense mechanism of the tissues of the host. Some types of bacteria have the ability to repel this defense and multiply rapidly while others are easily destroyed by it.

Cuts, abrasions, and other effects of traumatism upon skin and mucous membranes may permit the entrance and establishment of bacteria which otherwise would not occur. The age of the host has an important bearing upon the establishment of bacteria and production of disease.

As a rule young animals are more susceptible to infection than old ones. This is illustrated best by numerous diseases to which adults are resistant and children highly susceptible. Baby chicks are especially susceptible to Salmonella pullorum which produces a fatal septicemia and enteritis, while in the mature hen the organism localizes in the ovary where it causes a chronic type of infection. The reverse is true in avian tuberculosis which is found most commonly in old birds.

Malnutrition has a bearing upon the susceptibility of the host to infection. Vitamin D deficiency produces an increased susceptibility of respiratory mucous membranes to infection. Experimentally it has been possible to infect pigeons, which are resistant otherwise, with anthrax subsequent to a period of starvation.

Sudden and extreme exposure to cold has a bearing upon host resistance. Influenza appears in swine herds following sudden drops of temperature and exposure to cold, sleet, and rain. Hens which are naturally resistant to the anthrax bacillus may be infected with that organism when submerged in cold water which lowers their normal temperature.

The reverse effect of cold is noted in cold-blooded animals: frogs die quickly with "red leg" when kept in warm water, but deaths cease when the water is decreased in temperature by a block of ice.

The effect of fatigue on susceptibility is illustrated by the classical experiment of placing white rats, which are normally resistant to anthrax, upon a tread mill, and then injecting them with anthrax bacilli. After they have become fatigued, they will succumb to the disease.

The genetic constitution of the host is a factor in resistance. Strains of chickens which are resistant to Sal. pullorum infection have been produced by inbreeding; likewise, strains of mice which are resistant to mouse typhoid have been produced.

In summary, virulence depends upon, (1) the toxins and enzymes produced, (2) the number of invaders, (3) the specificity of bacterial products for certain types of tissue, (4) the inherent resistance of the host, and (5) the factors which alter that resistance.

Inasmuch as disease is an interaction between infective microorganism and host, we must examine the host more closely to see what characteristics are conducive to infection.

First, there is the problem of natural susceptibility as contrasted to natural resistance. This is one of the mysteries of disease and no one as yet has completely explained this mystery. In these days one hears the words "stress factors" so frequently. Twenty years ago we used to speak of these as "predisposing factors" and 100 years ago scientists used to think of them as the "definite causes" of disease.

The term "stress" can be extended to any factor whatsoever which seems to influence the establishment of disease in an animal. This means everything in the environment and inheritance of the animal. All of these things put a certain amount of stress on the living individual and may influence its susceptibility to disease. The air that it breathes, the food it eats, the temperature, the weather, the climate, the soil, the work, production, all exert an influence. The degree each exerts its influence produces disease variables and is difficult to measure.

It is always necessary to return to that very basic question of why one species of animal is susceptible to a given disease, whereas another is resistant. Again let me repeat that the answer lies in the mysteries of medicine. It is one of the evolutionary facts of science present with us today but which 10,000 years from now may be answered. As the intricacies of the chemistry of living things become revealed, answers to these questions may be forthcoming. In a rather elementary way then, let us look at the host to see what role it may play in the establishment of infection.

A discussion of the relationship of microorganisms to disease would not be complete without a brief description of the normal mechanism by which all animals are protected against infection. That this mechanism is an efficient one is apparent when one considers all of the possibilities of infection which animals encounter in their daily life. In fact, it is only when this natural protection fails to function that infection results. The type of tissue, the nature of secretions and their drainage, acidity, and alkalinity all function in normal protection against the infection.

The hair coat of mammals and the feathers of birds serve to protect the skin. The layer of epithelial cells of the normal skin constitutes an effective barrier against bacterial invasion. The skin of animals is constantly covered with bacteria which are potentially disease-producing when they invade the subcutaneous tissues. Many bacteria do penetrate into the crypts of sweat glands and into hair follicles from which they enter into deeper tissues. Even under such conditions they encounter an additional protective mechanism, the tissue phagocytes.

The epithelial covering of the mucous membranes also constitutes an effective barrier against bacteria. This tissue is constantly bathed in mucus which prevents bacteria from becoming established in crypts and folds. The mucous membranes of the eyes are continually washed by lacrimal secretion and those of the external genitalia and the urinary tract are periodically flushed with urine which prevents the lodgement of bacteria.

The mucous membranes, the mucus, and the tortuous characteristic of the nasal cavity protect the upper air passages against infection and also prevent the passage of dust particles into the lower part of the pulmonary system.

The trachea is lined with mucous membrane, and in the bronchi ciliated epithelium tends to sweep foreign particles outward. However, when bacteria surmount these barriers and reach the bronchioles and alveoli, infection results if they are in sufficient numbers to overcome the humoral and cellular defense of those tissues. The act of coughing makes it possible for bacteria to be carried outward in the mucus in which they have been entrapped.

The epithelial and mucous cells are most valuable barriers against infection throughout the digestive canal. Various secretions however, have a protective function in addition to being primarily concerned with the digestion of food.

Saliva has a feeble germicidal power and, in addition, keeps the mouth and esophagus bathed. Gastric juice is definitely inhibitory to many kinds of bacteria and their toxins because of the high hydrogen-ion concentration.

Arnold has shown that the pH of the upper part of the intestinal tract governs the bacterial flora found there and that alteration of the pH toward alkalinity causes the anterior movement of lower intestinal types of bacteria. The peristaltic movement of the intestinal tract prevents the lodgement of bacteria, and acculated masses of bacteria are dispersed by the constant mixing of the intestinal contents.

Previous mention has been made of the protective value of epithelium, mucous secretion, and urine lavage to the urinary tract and external

genitalia. These factors prevent the establishment of infection in such tissues unless there has been massive contamination.

The function of the urinary bladder as a collecting reservoir for urine prevents, except in rare instances, the ascent of bacteria into the ureters. The vital reproductive glands, testes and ovaries, are protected from external contamination by tortuous tubes which connect them with external parts.

In the female the ciliated epithelium of the fallopian tubes serves as a noteworthy obstacle to bacteria. In the pregnant animal the cervix is sealed with a tenacious substance which is a most effective protection for the developing embryo.

The eyelashes and eyelids protect the eyes against foreign objects which may be contaminated with bacteria. The voluntary response of lacrimal glands when foreign particles do reach the eye aids in diluting the invading substance, and if it is not too heavy or does not become lodged, will wash it away. The delicate mechanism of hearing is protected by the shell of the ear, the ear hairs, and ear wax. The invasion of the ear by bacteria from the exterior is extremely rare.

When infectious agents pass the barriers with which the body is endowed they then must survive another line of defense -- the humoral and cellular protective forces. This subject lies in the general area of immunology and it is beyond the time allotted for our discussion.

In summary, it has been made clear that the ability of the animal to resist infection is a formidable one, but the ingenious ways by which infectious agents gain a foothold are complex and not well understood. These are factors which make the study of infectious diseases so interesting and challenging. By continued research the infectious process will become more clear and then methods of prevention and cure will be more specific.

PATHOLOGY AND THE DIFFERENTIAL DIAGNOSIS OF TUBERCULOSIS

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It is generally recognized by animal disease regulatory officials that the follow-up tuberculin testing of herds based on the detection of suspected tuberculous lesions in non-tested cattle has proved to be a valuable adjunct to the tuberculosis eradication program. As a result of this procedure, nearly 15 percent of all tuberculin reactors are uncovered annually and new foci of infection are being discovered in unsuspected herds that might otherwise be a source of continued spread of the disease.

Unfortunately, not all infected animals found at slaughter are traceable to their source of origin due to inadequate means of identification. As improved methods are developed and more infected animals can be traced, the number of reactors will increase proportionately.

Prior to 1950 the follow-up testing of herds was pursued on the basis of the post mortem diagnosis of tuberculosis, and not infrequently particularly in range herds, the tuberculin test was negative. Such a practice is not without some chance of error, since there are a number of other bovine granulomas that are often grossly indistinguishable from tuberculosis.

In 1951, the Denver Laboratory of the Animal Disease and Parasite Research Division reported on a series of 77 visceral lesions of suspected tuberculosis found in non-tested cattle which were submitted for laboratory examination. This study revealed that 53 percent of the lesions were granulomas arising from other causes. The diseases most frequently confused with tuberculosis were actinobacillosis, mycotic infections, *Corynebacterium pyogenes* infection, parasitic lesions and carcinomatosis.

These observations were in part responsible for the issuance of a memorandum by the Meat Inspection Division in 1950 requiring laboratory confirmation of all suspected lesions of tuberculosis found in non-reactor beef-type animals before action is taken by the Tuberculosis Eradication Section.

As a consequence of that memorandum there was a marked increase in the number of lesions received for laboratory examination. While the majority of the specimens were from non-tested beef-type animals there were many lesions from dairy animals as well. This afforded an opportunity to examine an additional 418 cases received during the four-year period 1952 to 1956.

An analysis of the laboratory findings as shown in the table revealed confirmation of the post mortem diagnosis of tuberculosis in 227 cases (54.3 percent) as against the other diagnoses in 191 (46.7 percent). The same diseases showing gross similarity to tuberculosis were encountered in this series of cases as in the smaller group of 77 already mentioned.

In deference to the veterinary meat inspectors who submitted the specimens, the non-tuberculous lesions were in most instances grossly indistinguishable from tuberculosis and quite properly had been forwarded for laboratory confirmation. Conversely, lesions from nine animals were submitted with some other diagnosis which on laboratory examination proved to be tuberculosis (seven generalized). Among these were carcinomatosis, four, actinobacillosis, two, coccidioidal granuloma, two, and undetermined mycotic granuloma, one. Such discrepancies might

have been avoided if a diagnosis of tuberculosis had been given first consideration.

The post mortem diagnosis of tuberculosis in the bovine is usually based on the yellowish appearance of a necrobiotic process whether the lesion is caseous, caseocalcareous or calcified. This is a rather constant feature of a tuberculous lesion and even the purulent exudate in a larger lesion undergoing liquifaction necrosis remains yellow.

In contrast, the purulent exudate or pus of most of the other common bovine infectious granulomas has a greenish lustre which affords a basis for differentiation from a tuberculous process. Examples are the greenish viscid pus of actinobacillosis, actinomycosis, coccidioidomycosis, nocardiosis, mucormycosis, C. pyogenes and the inspissated pus of pentastome foci in lymph nodes.

Cancerous tissue (carcinoma) is commonly yellowish and is not infrequently confused with tuberculosis as indicated in the table. Metastatic lesions of carcinoma of the eye or the uterus may be mistaken for granulomatous tissue if the primary site is overlooked.

As the purulent content of the non-tuberculous granulomas is replaced by granulation tissue its greenish lustre gradually disappears, the lesion becomes a yellowish caseocalcareous or calcified type of tissue which has a strong resemblance to a tuberculous process. Even the greenish nodules in lymph nodes caused by migrating parasitic larvae may eventually turn gray or light yellow and be confused with tuberculosis.

Most of the common granulomas can be diagnosed by appropriately stained films, wet press preparations or by histological sections. Cultures or animal inoculations may be made for further confirmatory diagnosis if necessary.

The demonstration of acid-fast bacilli morphologically typical of M. tuberculosis in smears or in sections of a granulomatous lesion is generally acceptable for the diagnosis of tuberculosis. The presence of well defined rosette formations in unstained press preparations or tissue sections of a purulent or granulomatous lesion is indicative of either actinobacillosis or actinomycosis. Further differentiation of these entities can be made by stained smears, gram negative coccobacillary organisms being diagnostic for actinobacillosis and gram positive branching filamentous forms indicative of actinomycosis.

If spherules with a highly refractile double-contoured wall are seen in direct examination or on histological examination of a granulomatous lesion, a diagnosis of coccidioidomycosis can be made without additional laboratory tests. Likewise, a tentative diagnosis of mucormycosis or nocardiosis can sometimes be made by similar laboratory

procedures but the organisms are best seen in tissue sections and this is perhaps a better means of diagnosis.

A diagnosis of Corynebacterium pyogenes infection can be made by the demonstration of short gram positive pleomorphic bacilli in either stained smears or on histologic examination of the lesion. In older lesions the organisms may be sparse and difficult to find and cultures are advisable if sufficient material is available.

It should be mentioned that nearly all the 84 lesions diagnosed as C. pyogenes were examined histologically in search for acid-fast bacilli, since we were unable to demonstrate such bacilli in stained smears. We likewise failed to find acid-fast bacilli in tissue sections after prolonged search despite the microscopic resemblance to a tuberculous process of some of the lesions.

In nearly all instances however, residual foci of polymorphonuclear leucocytes were still apparent in the lesions, a feature not usually seen in an old tuberculous process. Whether some of these cases would have proved to be tuberculosis on culture or animal inoculation is problematic.

The most common parasitic condition encountered in this series causing confusion with tuberculosis is a lesion resulting from migrating linguatula larve. These are more often found in the mesenteric lymph nodes but are also occasionally seen in the thoracic chain of lymphatic glands. The larvae may also migrate in the mediastinum where they produce a greenish serous exudate which may extend into the adjacent interlobular spaces of the lung.

The greenish foci or nodules are more often located at the periphery of the affected lymph nodes and result from a heavy infiltration of eosinophils which represent a response to the dead and disintegrating parasites. Older lesions lose their greenish color, become gray or light yellow, and may undergo calcification so that they resemble a tuberculous lesion. The lesions are encapsulated and are easily shelled out in contrast to the fixed tissues in a tubercle.

We have failed to demonstrate the larvae or residual fragments in any of the lymph node lesions, and in only one instance was an intact parasite seen in the greenish inflammatory exudate in the mediastinum. Nine of the parasitic granulomas in this series were diagnosed as pentastomiasis, a term applied to this condition in nearly all meat inspection text books.

The other parasitic lesion shown in the table was a yellowish necrotic granular focus in the liver. There were no other visceral lesions in the carcass. Direct smears were negative for acid-fast bacilli. On histological examination the lamellar cuticle of a dead

and disintegrating echinococcus cyst was still apparent in the necrotic debris.

Two of the four staphyloccal abscesses involved the udder, and because of their yellowish granulamatous appearance tuberculosis was suspected. A pure culture of staphylococcus aureus was recovered from both lesions. In tissue sections, clumps of gram-positive cocci were present within ill-defined rosettes which were oontained in the purulent foci. This disease of the udder was formerly called botryomycosis but is now designated granulomatous staphylococcal mastitis.

The laboratory findings in 418 bovine granulomas in non-tested animals submitted with a suspected diagnosis of tuberculosis are presented.

The post mortem diagnosis of tuberculosis was confirmed in 227 cases-(54.3 percent) whereas 191 lesions (45.7 percent) were found to be other conditions.

The diseases most commonly confused with tuberculosis were caseocalcareous or calcified lesions of actinobacillosis, coccidioidomycosis, mucormycosis, and Corynebacterium pyogenes infection.

Neoplasms, particularly carcinoma, are often confused with tuberculosis and lesions produced by migrating pentastome larvae in lymphatic glands may be mistaken for tuberculosis.

The difference between the post mortem and laboratory diagnoses warrant continued laboratory confirmation of suspected lesions of tuberculosis, particularly when the follow up tuberculin testing of herds may depend on the diagnosis.

Laboratory Diagnoses of 418 Lesions from Non-Tuberculin Tested Cattle Submitted as Suspected Tuberculosis

	Cases	Percent		Cases	Percent
Tuberculosis	227	54.3	Mycoses	21[b]	5.0
C. Pyogenes	84	20.1	Parasitic	10[c]	2.4
Actinobacillosis . .	49	11.7	Staphylococcus . .	4	1.0
Neoplasia	22[a]	5.3	Streptococcus . . .	1	0.2

[a] Carcinomatosis 21, Mesothelioma of Peritoneum 1
[b] Coccidioidomycosis 12, Mucormycosis 4, Nocardiosis 2, Other 3
[c] Pentastomiasis 9, Degenerated Echinococcus Cyst of Liver 1

QUARANTINES

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It is believed that the first quarantines were put into effect when communicable diseases became recognized. One of the earliest was that against lepers. However, it was not until the year 1403 that quarantine procedures were instituted on a statutory basis. At that time the city of Venice, Italy, to protect itself against the 'plague' which had invaded Europe, adopted a regulation requiring all vessels from infected ports to be detained for 40 days in the harbor without communication with land or with other vessels.

The term 'quarantine' was thus derived from the Italian word "quaranta" meaning "forty." By coincidence it was at the time of the Lenten season which may have suggested the 40-day period. Some time later the City of Marseilles, France, provided the first definite code of quarantine when it introduced a "patente" or bill of health to be filled out by officials in ports of departure of vessels abroad, a practice which has been continued down to the present time. International quarantines are now applied not only to man, but also to plants and animals.

In combating most infectious diseases of livestock the stoppage of the movement of diseased and exposed animals can seldom be accomplished without some kind of quarantine. The principal object for the establishment of any quarantine is to confine the infection to the smallest possible area and to hold it there until it can be stamped out through the use of appropriate eradication measures.

It should be understood the efforts toward the control and eradication of communicable animal diseases within the different States are primarily the function of the respective State officials. The direct authority of the Federal Government extends only to control over the interstate movement of livestock from districts where any such disease is known to exist.

Authority to enforce local quarantines and to compel the destruction or the treatment of infected or exposed animals rests entirely with the States. Consequently, the work of Federal and State cooperative projects is done chiefly under State laws and regulations. Cooperative work, as contemplated by section 3 of the Act of May 29, 1884, is not undertaken in any State unless or until there are State laws and regulations which make it possible to apply established methods effectively and to protect the results achieved.

When the disease to be combated is not especially virulent and has not become widespread, it is possible to handle outbreaks by the application of State quarantines without the imposition of a Federal quarantine.

When the disease has become widespread and well established, however, local quarantines are not adequate especially when it is necessary to regulate the movement of livestock and vehicles used in their transportation from an entire State or a number of States. In such instances a Federal quarantine is imposed.

To be effective and to have the support of interested agencies, especially of livestock producers, quarantine measures must vary greatly and be appropriate for the particular disease that is being combated. They may range from a complete prohibition against the movement of all animals and vehicles and even restrictions on human beings, as in the case of an outbreak of foot-and-mouth disease, to a mere physical examination and movement under proper certification or official permit, as in the case of sheep and cattle scab, in which the animals are subjected to certain prescribed treatments that have been found to be effective.

Before we had quarantine laws, many animal diseases were introduced into the United States from abroad. At that time the animals went mainly to local markets for slaughter, so for that reason diseases did not spread rapidly. But with the further development of rail and water shipping, livestock in increasing numbers began to move from one State to another, and healthy animals were exposed constantly to diseased animals.

A few States undertook to control and eradicate contagious pleuropneumonia, but the only ones that succeeded by their own efforts were Connecticut and Massachusetts. The livestock industry became concerned at the spread of disease and recommended that the Federal Government take action to prevent further losses.

The Commissioner of Agriculture, in 1869, recommended to the Congress that a Veterinary Division be established to protect the Nation's livestock interests. By 1883, contagious pleuropneumonia had spread to most of the New England States and as far west as Ohio. The next year the livestock industry received Federal support in the control and eradication of disease, and the United States Bureau of Animal Industry came into existence.

While the Act of May 29, 1884, establishing the Bureau of Animal Industry, contained some authority for the expenditure of Federal funds for quarantine measures in cooperation with the States, it was not until the Act of 1903 was passed that the Secretary of Agriculture was given authority to seize, quarantine, and dispose of any hay, straw, forage, or similar material, or any meats, hides, or any other animal product coming from an infected foreign country to the United States.

However, the Supreme Court of the United States, in the case of Reid v. Colorado (187 U.S., 137) declared that the Act of May 29, 1884, conferred power upon the Secretary of Agriculture to institute quarantine measures only when the State affected had adopted the measures of the Bureau

of Animal Industry or when the Bureau of Animal Industry had approved the measures of the State looking to the suppression and extirpation of contagious diseases. It was therefore obvious that if contagious diseases of animals were to be controlled and eradicated in the United States, additional legislation was needed.

The Act of 1905 provided this when it authorized and directed the quarantine of areas in the United States infected with contagious livestock diseases and prohibited the interstate movement from such areas of any live animals except under such conditions as the Department may prescribe as safe. Usually the State involved places a quarantine on the same area so as to control the intrastate movement from the area under Federal quarantine.

To establish a Federal quarantine it must be shown that the disease exists in the area to be quarantined. This is the reason why Florida could not be placed under a Federal quarantine when cattle fever ticks were found there recently. Apparently the ticks involved were noninfectious since there were no death losses and no cattle were diagnosed as being affected with cattle tick fever. Under State quarantine and systematic dipping the ticks appear to have been eliminated.

On July 3, 1889, the first cattle tick quarantine order was issued to prevent the spread of the disease. However, it was not until 1906 that a concentrated effort to eradicate cattle fever ticks from the United States was begun.

The northern border line of the infected area was determined to extend as far up as Virginia and Tennessee. At that time 985 counties in 15 Southern States were placed under Federal quarantine because of tick infestation. By December, 1940, this area had been reduced to two counties in Florida and to parts of eight counties in Texas.

Complete eradication of the disease has been accomplished in the United States except for a 500-mile quarantine strip in Texas along the Rio Grande River, extending from Del Rio to the Gulf where reinfestation frequently occurs because stray and smuggled animals carry infectious ticks across the river to the American side. The fight to eliminate the cattle fever tick from the United States is probably the most extensive and sustained attack ever made on an animal disease. It certainly established the value of quarantine measures.

When the Bureau of Animal Industry was created, sheep scabies was prevalent throughout the sheep-raising areas. The first attempt to cope with the disease was begun in 1897 by controlling the movement of sheep in interstate and foreign commerce.

Control of cattle scabies through similar measures was undertaken in 1903. Since these measures did not accomplish the desired results, in 1905 a Federal quarantine was placed on a large part of the western range

area, and on other areas as required, and systematic eradication was undertaken. As soon as conditions warranted in any State or district, the Federal quarantine was removed.

At the present time there are no areas under Federal quarantine for sheep scabies in the United States. The last Federal quarantine, which was removed about a year ago, covered four parishes in Louisiana and $12\frac{1}{2}$ counties in Mississippi.

During the past few years cattle scabies has appeared in Colorado with the result that a Federal quarantine was established. Recently the last two counties in the State had the Federal quarantine lifted so that at present there are no areas in the United States under Federal quarantine because of cattle scabies.

In the tuberculosis eradication program there have been no Federal quarantine areas. Successful operation has been possible by placing complete dependence on State quarantines. The cooperative agreements in effect between the States and the Department have been implemented by State and Federal regulations which to a great extent have been based on the recommendations of the United States Livestock Sanitary Association.

While the campaign for the eradication of tuberculosis was at its heights, regulations were issued by cities, counties, and some States prohibiting the sale of any milk and other dairy products obtained from cattle other than those in tuberculosis-free herds. Although these were not technically quarantine measures, the results very noticeably hastened the work of eradicating bovine tuberculosis.

The operation of the brucellosis eradication program has been similar in many respects to that of tuberculosis in that no Federal quarantine areas have been established. Complete reliance has been placed on State quarantines, as well as State and Federal regulations governing the intrastate and interstate movement of cattle. As in the case of tuberculosis, some cities, counties, and States have issued regulations prohibiting the sale of milk and other dairy products except from brucellosis-free herds. This has stimulated interest in brucellosis eradication.

In 1952, after apparently being confined to California for more than 20 years, an outbreak of vesicular exanthema occurred. As a result, the disease has appeared in 264 counties in 42 States since the beginning of the eradication program in August, 1952. During the period from August, 1952, up to the present time Federal quarantine areas were established in 34 States. As of May, 1958, areas under Federal quarantine have been reduced to parts of four counties in New Jersey.

Scrapie in sheep has been another recent problem. Since the beginning of the eradication program in October, 1952, scrapie has been diagnosed in 19 States, and Federal quarantine areas were established in six

States. As of May, 1958, areas under Federal quarantine have been reduced to parts of two counties in Ohio.

The most recent disease problem of the Animal Disease Eradication Division is the screwworm project. A quarantine is proposed for the States of Florida, Louisiana, and Texas, and Arkansas during the months of May through October. It is planned to establish an inspection line along the west side of the Mississippi River from Memphis south, and on the southern Mississippi and Louisiana line. Regulations governing the interstate movement of livestock insofar as screwworms are concerned are being processed.

Quarantine measures used by the Federal Government in cooperation with State authorities have served with remarkable efficiency to prevent the spread of contagious diseases. The imposition of quarantines, while necessary to safeguard the livestock industry, tends to interfere in varying degrees with the operations of livestock producers, and should be imposed only when other means would be ineffective and lifted as promptly as conditions warrant. It would be impossible, however, to control and eradicate some of the contagious diseases in this country without the authority, both Federal and State, to impose quarantines.

SUSPECT CLASSIFICATION

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I believe you will agree I have been selected to discuss one of the most controversial subjects on the agenda. I do appreciate, though, the privilege of talking to you about suspect classification because if we were to poll all of you here, or poll any other veterinary group, we would probably find just about as many different opinions regarding this matter of suspect classification as we have individuals.

It is my personal belief, however, that at this period of our program, it is one of the items that should be given serious consideration if we expect to eventually come through with complete eradication. And, from listening to the papers and discussions so far during the conference, it seems that there is quite a growing attitude toward that final objective.

Most of our observations in regard to classification of animals in the suspect category have been made following accreditation of the country.

Actually, most of us were not too concerned with this matter prior to accreditation. During the initial phase of the tuberculosis program in the more heavily infected areas, the animal with a slight or questionable

response could be retained in the herd with assurance that a herd retest would soon be made as confirmation of its status, or if branded for immediate removal, the loss to the owner, compared to the added protection to his herd, was not serious. In the lightly infected areas, the few questionable responses played a minor role.

Today the story is changing in both types of areas. We are making every effort at this period of the program to locate that last infected animal. In order to accomplish this objective, every case which shows any response that cannot be declared an unquestioned reaction should be followed through to a final determination.

In all areas we continue to get responses that are not as definite as the veterinarian would like to see and he does not know just how he should interpret them. These are still of the same importance in our previous heavily infected areas and are of increasing significance in the initially lightly infected areas because marked changes are taking place in the agricultural field, especially in the Southern States where increased numbers of cattle from the breeding centers of the north central areas are being introduced for livestock development purposes.

In considering the suspect classification, we encounter two types of veterinary interpretation of this tuberculin response. There is the veterinarian who worked in the earlier days when there was a heavy incidence of tuberculosis. He is following the policy of making a personal evaluation of all tuberculin responses. He may be reading the test in a herd where there are several responses and say "Now with this animal, the response is very typical but with this other animal, the reaction, in my opinion, isn't typical so we'll forget her." Or he may identify a single case of the latter so-called a typical reaction and pass the herd without reporting the condition.

I don't think we can follow that policy any longer. If we are going to leave such an animal, let's identify her as one that needs some reconfirmation. Let's not say she is definitely not tuberculous.

Then we have the other veterinarian working with us today who has unfortunately never had much field experience and who is following the basic guide lines which have been provided as instructional material for the testing program. He does not possess the advantage of training which permits him to use professional judgment in his final decision as to whether the case should be diagnosed as a reactor animal or one which should be given some further study.

For the time being, this veterinarian is operating more nearly as a trained lay technician. In any case, where there is an obvious tuberculin response not classified as a reaction, the animal should be classified a "Suspect" and subjected to retest by a qualified, experienced veterinarian.

In Michigan, we use our own State and Federal full-time veterinary personnel for follow-up testing on all suspect cases. Also, when an animal is designated a suspect, it should be placed under quarantine to assure that no unauthorized movements will be made. This, I believe, is not common practice, and until recently, was not the procedure in our own State. Now, however, we place these animals under quarantine and apply a retest at the end of a 60- to 90-day period.

In most instances, while it is not so stipulated in the regulations, a retest is conducted on the entire herd. In all cases where an owner elects to dispose of a suspect for immediate slaughter under permit, a retest of the other herd members to determine the possibility of herd infection is mandatory. By encouraging the reporting of suspect animals and providing for a complete herd retest, we are confirming in the interest of the owner and the program the status of the herd about which there is some question.

Without declaring suspects, there is a tendency on the part of many owners to move animals which they know have created some question in the mind of the veterinarian and unfortunately these may pass through a commission sale for return to another farm. Without protection afforded through the classification, recording, and quarantine of such animals, we are suffering a definite weakness in our program.

Let's encourage our veterinarians to report them as such without thought of embarrassment and with assurance that they are protecting the interests of their client and the future of the program. The whole policy of classifying animals under test as either reactors or negative just does not fit into our present age and goal of eventual eradication.

CURRENT RESEARCH ON BOVINE TUBERCULOSIS

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I will briefly discuss some of the research on tuberculosis that is presently under way and explain the reasons for these lines of approach. Research will, of course, increase our knowledge of tuberculosis. However, I would like to point out that we should not pin all our hopes on techniques not yet developed. Let's first be certain that we are using all methods and experience available to us to the best possible advantage. As an example: the intradermic injection of tuberculin must be performed carefully and accurately. In applying the test we are dealing with a degree of allergy in the animal that demands extremely critical and meticulous techniques to detect. Unless the test is carefully applied and the

results interpreted with extreme care and professional judgment, it is of little value. Future research will not compensate for careless application and interpretation of the present tuberculin test.

The tuberculin presently in use is the best available. It is standardized so that the recommended dose will produce a reaction in most infected animals. Occasionally, infected animals may fail to react because their sensitivity to tuberculin is so low that the standard dose will not detect it.

In research on tuberculosis we must remember that in addition to *Mycobacterium tuberculosis* var. *bovis*, there are other bacteria belonging to the genus *Mycobacterium*. This genus is a man-made classification of a number of species of bacteria that have certain characteristics in common and the species "tuberculosis" is further subdivided into three varieties. These closely related bacteria contain certain proteins which appear to be identical. For instance, a tuberculin made from *M. tuberculosis* var. *bovis* contains certain protein components which might elicit reactions in animals that are infected with other species of *Mycobacterium*. However, we think that each species and variety also contain proteins which are found only in that species or variety. Such proteins would be called specific proteins. If these specific proteins could be isolated chemically we would have an even more specific diagnostic product for cattle infected with bovine tuberculosis. We are working on the hypothesis that such proteins are present and can be isolated.

We have been discussing the bacteria and their products, now let us discuss the infected animal or host. Since it is infected with a species or variety of *Mycobacterium* it may be sensitized by the various proteins composing the bacillus. This may complicate the problem of developing a specific test product. Research in this country and Great Britain has shown that certain protein fractions of tuberculin when injected into artificially sensitized animals are quite specific. However, when these same products are used in the field on naturally infected animals the specificity is no better than the present tuberculin. One of these products is a purified protein derivative of tuberculin (PPD).

If a pure protein that is specific for bovine tuberculosis can be isolated we may have one of the answers to the problem of tuberculosis eradication.

Another line of research currently in progress is the hemagglutination test for tuberculosis. Dr. Larsen and his associates at the ADP Regional Animal Disease Research Laboratory at Auburn, Alabama, have been working with this test for several years. The present status of the work suggests that we are approaching a practical test which may do for tuberculosis what the ring test has done for brucellosis. If the hemagglutination test can be perfected, blood samples obtained for routine brucellosis testing could be checked by this particular test for the purpose of spotting

tuberculosis infection and thereafter followed with an intradermic tuberculin testing of the suspected herd.

The hemagglutination test is a modification of the one mentioned earlier in the program. Red blood cells of sheep are sensitized with PPD tuberculin or a similar product. Serum to be tested is first exposed to non-sensitized erythrocytes to remove certain non-specific material. The sensitized cells are then exposed to the serum and incubated to complete the test. Sera from infected animal agglutinate the sensitized cells.

Another promising bit of research has to do with tissue culture. HeLa cells are now being used to grow Mycobacterium tuberculosis var. hominus. This method appears to have advantages over those currently in general use for isolation of this bacillus. Additional work is now under way on this procedure which may be helpful in the overall problem.

In closing, I would like to emphasize that more knowledge of tuberculosis is needed to assist us in eradicating the disease. But, in the meantime, it is necessary to make full use of all knowledge presently available. An example of this is the Cache Valley problem in Utah. Originally it was thought that tuberculosis did not exist in that region and tuberculin reactions in cattle there were from unknown causes. However, a careful study of the problem revealed the presence of both avian tuberculosis and Johne's disease, both of which may cause animals to elicit reactions to standard tuberculin.

RETEST SCHEDULE AND FOLLOW-THROUGH ON PROBLEM HERDS

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The retest schedule is followed in most States in accordance with the uniform methods and rules set forth by the U. S. Livestock Sanitary Association. The variance is mostly concerned with the number of tests required following disclosure of reactors to release the quarantine and drop the herd from the retest schedule.

There are three main categories for classifying the retest schedules: The Non-Gross Lesion (and skin lesions only) cases fall in the first category. Some States, including Michigan, release the quarantine on one negative test with a follow-up test in six to nine months.

The second, or Gross Lesion category shall receive a minimum of two consecutive negative complete herd retests covering a period of five to six months from the date infection was discovered before being considered for a quarantine release. In herds with a history of heavy infection, or in an area where heavy infection involves many herds, a third negative

test would be advisable before the herd is released from quarantine. In either case, a follow-up negative test should be obtained six months later before the herd is dropped from the retest schedule.

The third, or suspect herd category, can be a dangerous classification if misuse is made in classifying reactors disclosed. This category should be held to a minimum and used only when herd history and other factors indicate a need. In most States (including Michigan) only the suspects are quarantined and the rest of the herd is free for movement into other herds.

We recommend a complete herd retest where suspect animals have been declared, including verification that the suspect animals were present for test. If not present, disposition of such animals should be determined. We would certainly expect a retest on the balance of the herd in any case where these suspects have been moved out.

There are possible situations where a retest of the suspect only might be accepted. An animal which has recently been purchased and has not yet mingled with the herd, and a large beef herd on pasture with the suspect animal in isolation are examples of such exceptions.

All retests for tuberculosis should be conducted with a minimum of 60-day intervals. A review of records should be made periodically and regularly to avoid omission of assignments. A complete review and study of the records should be made to learn all of the previous history. Promptness in conducting tests after the due date contributes to good disease control and good public relations with the herd owner. The high and low injection is recommended on all infected herd retests and also on suspect retests. The use of the cervical test is also recommended in herds so warranted as has previously been discussed.

There are different types of problem herds involved in our program. For example, there is the herd with a Gross Lesion history and which continues to have reactors. Another type is the herd with no Gross Lesion history and which continues to have reactors. A third type is the one showing problematical tissue disturbances of unusual character.

In the latter classification, the operator's technique and equipment should be observed. We further recommend that all disturbances be recorded and reported and not merely ignored.

The cleaning and disinfection of premises are important factors to study. A thorough investigation of the entire premises will often reveal some information otherwise missed. As much time should be spent with the owner as he is willing to sacrifice and we are of the opinion that if inquiry is made into all phases of the farm operation, a solution to the problem will be revealed. Some of the considerations to be checked with the owner are:

1. Poultry and swine on the premises at present and in the past and the degree of contact with the cattle.

2. Possible human sensitization, both by the family and possible exposure from outside individuals.

3. Inquire as to how thorough previous cleaning and disinfecting has been carried out.

4. Inquire into the agents used and previous procedures followed.

5. Check into the possible contamination of feed by use of alley carts and other equipment.

6. Check into the water supply and possible contamination.

7. Make inquiry into health status of all present and previous hired help.

8. Determine the possibility of premise contamination by commercial vehicles such as livestock trucks, tractors and feed grinders brought on to the premises.

9. Inquire into the source of purchased feed supplies, including milk products for feeding calves.

10. Check on any additions to the herd and determine contacts with neighboring herds.

11. Check on cattle that may have been away from home on exhibition or for any other purpose.

12. Determine if there has been any manure or poultry litter brought on the premises from outside sources.

13. Determine the possibility of wild game being a factor, especially pheasants and pigeons.

Going into all these phases takes time and patience but it may be very beneficial and pay off as many other things will come up in such a discussion with the owner. Often valuable information is disclosed that may lead you to the seat of trouble and consequent eradication of the disease in the herd.

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PARATUBERCULOSIS

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Johne's disease has been reported from many countries throughout the world. It has been diagnosed in more than 500 herds in the United States, and evidence at hand indicates that it is continually spreading and probably exists in every State. The shaded areas on the map (figure 1) represent counties in which Johne's disease has been diagnosed in one or more herds of cattle.

Additional infected herds probably would be found if more testing were done and the disease reported each time it was diagnosed. Estimates of losses from Johne's disease in infected herds may involve uncertainty since they so often depend on a herdsman's memory as to actual cause of death. However, losses may be greater than the owner thinks.

Actual loss encountered in a herd of purebred Guernseys consisting of 100 adult animals and 67 young stock was studied by U.S.D.A. workers for 12 months. No attempts at control were made. Of 18 animals culled during the year, 7 were eliminated because of Johne's disease. That's as many head as were removed for reproductive disorders and more than the total taken out for all other reasons.

Salvage for these 7 animals was estimated to be $1,300 less than their value as dairy animals. Johne's disease probably shortened each of their lactation periods as much as 6 months. Milk was bringing about $25 a head monthly over feed costs for each animal, so the total milk production loss amounted to $1,000. In addition to these losses, the owner was advised against selling surplus heifers for dairy purposes because of the diseased condition of the herd. This resulted in an additional loss. Such losses continue year after year unless the disease is brought under control.

The impact of Johne's disease on the agricultural economy of a number of European countries is so severe that the European Productivity Agency recently sponsored a seminar on the control of the disease, which was attended by personnel from 10 countries belonging to the "Organization for European Economic Co-operation."

Johne's disease is described as a chronic infectious disease of cattle, sheep, and goats, characterized by inflammation of the intestines and a recurrent diarrhea that may persist for months. Ruminants are the only animals that have been found to be susceptible to infection.

Johne's disease is caused by a small, rod-shaped, acid-fast bacillus named *Mycobacterium paratuberculosis*. This organism has staining characteristics identical with those of the tubercle bacillus, the Ziehl-Neelsen staining procedure being used routinely.

The bacteria attack the intestinal wall, where they are usually found in clumps. They are most often found in the posterior part of the small intestine, ileocecal valve, the large intestine, and the rectum, although they may also be found in the adjacent mesenteric lymph glands.

M. paratuberculosis is very difficult to culture on artificial media. A detailed discussion of culturing techniques is not within the scope of this paper. Briefly, the infected tissue is minced and mixed with antiformin or an acid to destroy all except acid-fast bacteria. The treated tissue is placed on media containing dead acid-fast bacilli or extracts of them. Other ingredients of the media are variable depending on the bacteriologist who is attempting the isolation.

Chemical analysis shows that M. paratuberculosis, like other mycobacteria, contain a relatively large amount of fat and wax. About 50 percent of the weight of fat-extracted bacilli is protein. In addition, they contain carbohydrate, phosphorus, magnesium, sulfur, potassium, sodium, calcium, and iron in measurable amounts.

The bacillus survived 270 days when stored in tap water, pond water, or distilled water, 246 days in bovine feces, and only 7 days in bovine urine. It has been found to survive 47 months in a desiccated state and at least a year in a cold-storage freezer at -14° C. Bacilli placed on filter paper and exposed to sunlight through cellophane were viable after 65 hours of exposure, but not after 100 hours of exposure.

The effect of various disinfectants has also been studied. Cresylic disinfectants are as effective against M. paratuberculosis as they are against M. tuberculosis. In dilutions of 1:32 they destroyed M. paratuberculosis in 15 minutes. Sodium orthophenylphenate destroyed the bacillus in 15 minutes in a dilution of 1:200. This product has no objectionable odors and is not expensive to use.

Products that did not destroy the bacillus were 6 percent sodium hydroxide solution and quaterinary ammonium solutions containing 1:250 available quaterinary. It required 14,000 ppm available chlorine to destroy the bacillus. This is about 150 times the usual concentrations used for disinfecting premises.

The bacillus is disseminated in the droppings of infected animals, and susceptible animals become infected by ingesting the contaminated droppings in the feed and water. Evidence is also accumulating that indicates infection can pass from a dam to unborn offspring.

The disease is not readily transmitted from herd to herd except through traffic in diseased animals, as shown by a survey conducted on 170 diseased herds. In a number of herds in which the survey was made, the method of introduction was unknown, but where information was available, in all instances except two the disease had been introduced by the

purchase of infected animals. The two exceptions were instances in which drainage from infected premises in the vicinity was suspected.

Experimental transmission of the disease can be accomplished by feeding susceptible animals infected mucous membranes and by feeding or injecting virulent bacilli intravenously. Results of infection experiments show that young animals are much more susceptible to the disease than mature animals. It has also been shown that the incubation period is a year or more unless an unusually large inoculum is given.

Clinical symptoms are usually observed in mature animals between 2 and 5 years of age. Symptoms are first observed in females within a few weeks after calving. Males may break at any time during the year, usually after a heavy breeding season.

The usual symptoms are a persistent diarrhea without straining, which responds only temporarily or not at all to the usual treatments for that condition. A rapid loss of flesh and tight skin accompanies the diarrhea. However, the temperature remains normal, and the affected animal continues to have a good appetite until the terminal stage of the disease.

Occasionally, the diarrhea stops, weight is regained, and the animal shows improvement, but such improvement is usually of a temporary nature and the animal begins scouring again and eventually dies. An alert herdsman may notice a gradual loss of flesh and diminished milk flow a month or more before the actual diarrhea begins.

Johne's disease can be confused with parasitism, malnutrition, acetonemia, and hardware disease, and may be diagnosed as one of these conditions if a hasty diagnosis is made.

Apart from the general lesions of emaciation, specific pathological changes are usually confined to the intestine and associated mesenteric lymph nodes. The intestinal wall is thickened, and the mucous membrane is found to be abnormally corrugated or wrinkled. Evidence of ulceration or erosion is not found, but the mucosa may show areas of congestion. The ileocecal valve may be swollen and congested. Macroscopic post mortem findings are undependable for diagnoses because intestines from diseased animals sometimes appear normal.

Histological examination shows the invasion of the infected tissues by large numbers of cells of an epithelioid nature. These lesions may extend into the submucosa. The bacilli may be extra-cellular or intracellular and may also be found in adjacent lymph nodes.

A tentative diagnoses of Johne's disease can be made by observing typical clinical symptoms of the disease. However, this must be confirmed by obtaining a positive johnin test, and by finding the typical

small acid-fast bacilli in stained smears prepared from rectal mucosa or feces or histological sections removed from the intestinal wall and adjacent lymph glands. Rectal mucosa can be obtained from a living animal by inserting the arm deep in the rectum and scraping the bowel wall with a finger nail.

Failure to find organisms in smears prepared from rectal scrapings or feces does not justify a negative diagnosis, and the animal should be under suspicion and isolated until the cause of the illness has been determined. If the animal is suffering from Johne's disease, it will usually die and the bacilli can be found in smears or histological sections prepared from the intestine and lymph glands post mortem.

If the person attempting to make the diagnosis is not equipped to make a microscopic examination, he should send specimens to a diagnostic laboratory. The specimen should consist of 24 inches of large intestine containing the ileocecal valve and about 12 inches of attached small intestine along with adjacent mesenteric lymph nodes.

Diagnostic agents play an important part in diagnosing the disease. Both johnin and avian tuberculin have been used subcutaneously, intravenously, and intradermally as diagnostic aids. The intradermic test with johnin is less time consuming, as accurate as other methods, and is the test commonly employed by the Animal Disease Eradication Division and State livestock officials.

The test is conducted by injecting 0.2 cc of johnin into the skin of the caudal fold or the cervical region. The cervical region is more sensitive to johnin than any other skin area of the animal's body, including the caudal fold. A positive reaction consists of a slight swelling similar to a tuberculin reaction 48 hours after injection. The swelling tends to be softer and more diffuse than the swelling due to injection of tuberculin.

There is still a recognized need for a more sensitive and specific test for use in herds where Johne's disease is particularly difficult to eradicate and to differentiate from sensitizations caused by other acid-fast bacilli. Investigations of possible diagnostic procedures have involved allergic and serologic studies. In the development of allergins, *M. paratuberculosis* culture filtrates have been purified and fractionated to obtain a more specific and potent product for intradermal testing. Many products have been prepared but very few show promise.

In the development of serological tests, complement-fixation and hemagglutination reactions have been tried. Various types of antigens have been used in the complement-fixation test. It has been found that the complement-fixation test is sometimes positive in animals that are not infected with an acid-fast disease. However, it has an advantage in that sera from an animal in advanced stages of the disease may show

a positive titer even though the animal does not react to intradermal johnin.

A modification of the Middlebrook-Dubos hemagglutination test has been used for diagnosing Johne's disease. This test is conducted by sensitizing sheep erythrocytes with johnin PPD. The sensitized erythrocytes are mixed with sera from suspected animals and observed for evidence of agglutination. The test may show positive results in animals infected with tuberculosis, which of course is a disadvantage. The hemagglutination test can be further modified by the addition of complement and read as a hemolytic test.

At present, research is under way to evaluate these tests by correlating them with post-mortem findings. However, the following observations have been made from results obtained thus far: (1) It is unusual for animals in herds free of Johne's disease and tuberculosis, to show hemagglutination titers higher than 1:16 or complement-fixation titers of 1:4, and (2) Infected herds invariably contain animals showing hemagglutination titers of 1:32 or more and complement-fixation titers of 1:8 or more.

Products which have shown marked therapeutic effects on tuberculosis and leprosy have been tried for the treatment of Johne's disease. Streptomycin, isonicotinic acid hydrozide, and 4:4' diamino diphenyl sulfone have each been tried on a limited number of animals showing clinical evidence of the disease. None of these products have cured an animal although temporary improvement was noted in several instances.

Immunization against Johne's disease is being studied in a number of countries. The vaccine is usually made by suspending M. paratuberculosis in an excipient that is not absorbed, such as mineral oil. A fibrocaseous nodule is formed at the site of injection.

Vaccination experiments conducted on thousands of sheep in Iceland indicated that marked protection against Johne's disease was established. The vaccine may cause vaccinated animals to react to the tuberculin test, which is a serious drawback to its use in cattle. Since cross reaction to tuberculin is not an important factor in sheep, we have a limited field trial of the vaccine under way in the United States in an infected flock of sheep.

The disease causes sheep to lose condition over a period of time as it does cattle. However, diarrhea is not as marked. The bacillus causing the disease in sheep can be demonstrated in smears or histological sections from the intestinal tract as in cattle. Infected sheep also react to all the diagnostic tests previously described. It has been found to be very difficult to control the disease in this species.

When Johne's disease is clinically diagnosed in a single animal, all the animals in the herd should be tested with intradermal johnin.

If the number of reactors is only a small percentage of the herd, they should be removed at once and slaughtered.

After the animals have been removed, the premises should be disinfected by the same procedure used in disinfecting premises from which tuberculin reactors have been removed. All manure and a thin layer of top soil should be removed from lots used by infected animals, and lots should be arranged in a manner to allow direct exposure to sunlight at some period of the day.

If a large number of reactors is disclosed, the owner may not wish to assume the heavy loss that would result from immediate slaughter. He should be advised to eliminate any animals showing clinical evidence of the disease at once, and to dispose of the remaining reactors by slaughter as rapidly as he can raise young animals for replacement. This procedure, of course, involves a risk as reacting animals may be spreading the disease. Breeding stock should not be sold from a herd in which reactors are retained.

The key to the successful control program is to prevent susceptible animals from ingesting infective droppings along with feed and water. Since calves are easily infected, they should be removed from their dams within 12 hours after birth and placed in separate quarters. Attendants caring for these calves should disinfect and clean their footwear each time they enter the quarters. The calf-rearing quarters should be provided with separate cleaning and feeding equipment, and such equipment should never be exchanged with equipment used for mature animals.

Feeding and watering equipment for all cattle should be constructed so as to prevent fecal contamination of the contents. Equipment used for cleaning manure from stables should never be used or stored in feed rooms or feed alleys, and attendants should change or disinfect footwear before proceeding from areas contaminated with manure to feed rooms.

Suitable disinfectants in foot baths should be placed at the entrances of feed alleys and feed rooms, and attendants should be instructed to use these facilities. Johnin tests should be conducted on all animals in the herd at 6-month intervals. If negative results are obtained on three successive tests and no clinical symptoms of the disease observed in the meantime, the herd may be considered clean.

FIGURE 1.—Distribution of Johne's disease in the United States. Shaded areas represent counties in which the disease has been diagnosed in one or more herds of cattle.

COLLECTION OF SPECIMENS FOR LABORATORY DIAGNOSIS OF TUBERCULOSIS AND PARATUBERCULOSIS

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In order to assure accurate diagnosis, the collection of specimens must be carried out in such a manner as to assure no contamination. Also, the specimens must be collected with considerable precision to prevent excessive slowdown of the operations of the packing plant. This calls for considerable prior planning. Only those herds in which considerable trouble is being experienced should be used for collection of specimens. This is made necessary by the limitation of our facilities at the present time.

Prior to testing the problem herd and making final arrangements, a shipping container should be ordered from our laboratory. The laboratory's address is as follows: ADE Diagnostic Laboratory, Veterinary Quadrangle, Ames, Iowa.

The shipping container is an insulated chest holding enough bottles for specimens from about two or three animals. Knives and forceps will be enclosed for your use.

After receipt of the chest final arrangements must be made for testing and collection of tissues from suspicious herds. This includes contacting owner, trucker, packing plant and veterinarian in charge of meat inspection. Although only a brief mention of the original arrangements is made here, making the necessary arrangements will determine the success of the project. In some instances almost split-second timing will be needed to prevent unnecessary slowdown of work at the packing plant.

Upon receipt of the box, it will be necessary to procure formaldehyde, 70 percent alcohol, and sterile cotton. All of these items can be obtained at a drug store. The formaldehyde is usually sold in 38 percent solution. By taking 10 ml. of the 38 percent solution and adding 90 ml. of water the formaldehyde will be of proper strength for use in preserving tissues for histopathological studies.

It will be noted that the shipping container holds two sizes of specimen bottles. The large (4 ounce) bottles should be filled with the above-mentioned formaldehyde solution (10 ml. 38 percent formaldehyde, 90 ml. water). The bottles should not be completely filled. About one-tenth of the space in the bottle should be reserved for tissue. In other words, tissues should be placed in about ten times their volume of formalin.

Tags should be obtained for identifying all tissues submitted. These can be marking tags with string attached. A portion of the string can be placed in the tissue bottle and the cap screwed down tight to secure the tag. The tags should be marked so that the marking will not smear if it becomes moist in shipment. The tags should be marked with the reactor tag number of the animal and the anatomical region of the animal from which the tissue came.

Tissues from each animal should be collected from the lymph glands of the head, thorax, abdomen, and the body, including the supra-mammary.

This does not mean all glands, but portions of representative glands of each region.

In removing the glands a separate, sterile knife and forceps should be used for each of the four regions of the animal. This means that those instruments not being used should be kept in the 70 percent alcohol when not in use. As they are needed they are removed from the alcohol and wiped dry with sterile cotton.

As each gland is removed with sterile knife and forceps, a portion of it is placed in one of the small jars and another portion in one of the larger jars containing formalin. The jars should be immediately identified with tags. If any of the glands have lesions, an attempt should be made to send a portion of the gland which appears normal as well as part of the lesion.

After the specimens have been collected those jars containing formalin and tissue should be removed and packed in a separate box for mailing to the laboratory. The tissues in the formalin should not be frozen. Freezing will destroy the cell structure and make diagnosis difficult.

The tissues placed in the small (2 ounce) dry jars should be placed in the insulated box and packed in dry ice. These tissues are to be used for culture work and freezing will not destroy the tuberculosis organism. Dry ice will prevent decomposition of the tissue for at least 36 hours.

The tissues placed in the insulated box must be shipped air express. This means that air schedules for express must be checked to make sure that the tissues arrive at the laboratory within 36 hours after mailing. The laboratory should be notified as to the exact time of arrival of the tissues at the Des Moines Airport. The box should be labeled as follows: The Director, ADE Diagnostic Laboratory, Veterinary Quadrangle, Ames, Iowa. In addition, the box should be marked "Hold at airport in Des Moines."

Each of the two boxes containing tissues should also include the name and address of the shipper, the name and address of the owner of the animals from which tissues are submitted, the disease suspected and whether typing of any tuberculosis organisms recovered is desired, and a complete history of herd. The box containing the tissues in formalin can be shipped by parcel post.

The foregoing has dealt mainly with tuberculosis. In paratuberculosis, or Johne's disease, small sections of intestine, particularly near the ileo-cecal valve, and including all of the layers of the intestine, should be sent. It would be well to include a few mesenteric lymph nodes. These specimens would be mailed air express under refrigeration. A similar group of tissues (intestine and lymph nodes) should be formalized as described previously and mailed parcel post along with complete information on each shipment.

THE PRINCIPLES OF EPIDEMIOLOGY

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Epidemiology is that body of knowledge, that science, which underlies the whole field of public health. An adequate public health program requires the services of many separate but related professions including human medicine, veterinary medicine, sanitary engineering, statistics, nursing, the social sciences and many biological services. All need to have a general understanding of epidemiology to function effectively.

A close bond of common understanding and a long record of successful working relationships exist between the physician and the veterinarian in public health. This common bond is perhaps closer than that to most other public health professions because both the physician and the veterinarian have a broad common background of training in the same basic sciences of medicine, anatomy, bacteriology, pathology and physiology and really very similar types of experience in clinical work.

At the Communicable Disease Center, the veterinarians, under the leadership of Dr. James Steele, and the medical epidemiologists have worked together in the closest harmony in a fully integrated program for the past decade.

The word epidemiology has been difficult to define in a meaningful way because it is often used in two different senses, a broad one and a narrow one. The broad meaning of the word includes such phrases as the natural history of disease, human ecology, or even the philosophy of disease. These all-inclusive ideas may sound impressive but do not impart a very clear idea of the duties or functions of the epidemiologist nor do they delimit his sphere of interest and responsibility from other medical specialists.

The narrow meaning of the word is best illustrated by considering what the epidemiologist actually does and what services and operations he actually performs in the discharge of his duties.

The closest analogy can be made with the clinician or the practicing physician. His is a highly individual job. He must diagnose and treat patients one by one.

The epidemiologist, on the contrary, must be concerned with populations, whole communities at a time. He studies the occurrence and distribution of disease among groups of people. His diagnoses must be the source of infection and the mode of spread. His treatment must be the institution of control procedures.

The term epidemiology derives from the Greek word epidemos, meaning upon or among people. Formerly the term epidemiology was restricted to

the study of epidemics. It was a descriptive, almost narrative discipline, in which simple accounts were made of the plagues and epidemics that often were so devastating.

With the advent of modern biological science, especially bacteriology, epidemiology became the science of the occurrence and spread of endemic as well as epidemic disease. More recently, especially in the last decade or two, the term has been widely applied to the study of the community or group aspects of all types of disease, including heart disease, cancer and even automobile accidents.

With all this broadening, the term is still limited to those factors that influence the occurrence of disease among people. Epidemiology remains a collective science dealing with both the sick and the well and their relationship to each other and to their environment.

In its early descriptive phase, epidemiology considered the problem of disease as something imposed upon man from outside, from some external or even supernatural forces. As bacteriological knowledge grew, this highly egocentric view tended to persist.

The parasites causing disease were more specific forces than were formerly recognized but tended to remain simply as undesirable factors that should be eliminated. Slowly more fundamental biological concepts developed which now are broadly recognized as forming the very foundation of epidemiological thinking. These concepts view infectious diseases as basically one manifestation of the more general phenomena of the host-parasite relationship or ecology. Hence the popular definition of epidemiology as human ecology.

In this modern view, man is but one species of animal that has survived over the centuries by natural selection and adaptation. Likewise all other animals, plants and microparasites have adapted and survived.

Disease becomes an intrinsic feature of the biological interaction of species competing with each other. Those that have survived have achieved some sort of balance in nature. Thus epidemiology may well be defined as that science concerning the factors which determine the biological balance between the host and the parasite.

Dr. Theobald Smith, a veterinarian and one of the greatest epidemiologists, was a leader in the development of this biological concept of epidemiology, which he outlined in a series of lectures at Princeton University some 30 years ago. He clearly expounded the concept of the chain of infection and visualized four distinct links. To survive, a parasite must (1) Gain entry into a host; (2) Multiply within the host; (3) Achieve exit from the host; and (4) Transfer to a new host.

When first formulated, this concept of the chain of infection was most useful because it helped in planning and directing control efforts.

These could be directed toward the weakest link. Certainly in some diseases one or two links were more subject to attack than others.

With experience however, the concept is clearly oversimplified. It is not necessary to break even a single link to achieve effective control. Actually weakening one or several links has been sufficient. The biological balance is a more complex and intricately interrelated process than the elementary concept of a chain.

The broad objective of epidemiology is a subject of special interest to veterinarians as well as others of the public health profession. A major difference of opinion now exists among epidemiologists. One group believes the only logical objective of the science is the eradication of all undesirable parasites. The other group doubts that such an objective is either realistic or desirable.

The first group argues that the biological balance between man and his parasites is subject to intensive study and that man should be able, through wise application of knowledge, to totally disrupt the biological balance so that parasites cannot survive.

The second group argues that the balance has been achieved over many centuries of adaptation and that such forces cannot readily be disrupted. Rather they argue that the objective should be to use knowledge to tip the balance in favor of man with the hope that disease will progressively decline but with the understanding that this decline will probably be slow and incomplete, or at best only approach the zero base line asymptotically.

Many examples to support the arguments of both groups can be chosen. Often discussion of these intriguing ideas founder on the issue of semantics. The issue is great enough, however, to command serious thought of all epidemiologists and those concerned with public health in the broadest sense.

With regard to the semantic problem, the word eradication in the literal sense, applied to any disease throughout the world, clearly is a big order, although it is now being seriously discussed for malaria and for smallpox. The proponents of the eradication objective choose to limit the term geographically to any reasonable population group, say a whole country, a major river valley or a continental land mass. This concept of "area eradication" makes possible a more limited but realistic discussion of the subject.

Those who argue against the eradication objective have a series of examples of frustrations to quote. For instance the Rockefeller Foundation once sponsored a program for the eradication of hookworm, only to find that the combination of social and biological factors involved exceeded the capability of an organized program to conquer.

Hookworm infection still exists in many parts of the south although hookworm disease is rare. The yellow fever eradication campaign offered grand hopes until the existence of another mechanism of survival in the form of jungle yellow fever was discovered.

At one time it seemed probable that typhoid fever might be eradicated through basic sanitation of water and food supplies, but later the discovery of the capacity of the typhoid bacillus to colonize the gall bladder revealed a new long time survival mechanism. Similarly the rickettsia of Old World typhus was discovered to have a capacity to lie dormant in the human host for many years, later to manifest itself as Brill's disease.

These and other examples have led many epidemiologists to develop a wholesome respect for the forces determining the biological balance to the point where some have tended to generalize that eradication is not a tenable objective.

The proponents of the eradication objective on the other hand, applying the concept to defined areas rather than the whole world, remain confident. They look at cholera that once was a devastating epidemic disease in western Europe and America, but which has not been known there for half a century. They look at urban yellow fever that has been eliminated from North America and the Caribbean cities and claim that a very substantial measure of area eradication has been achieved.

During the past two decades smallpox and malaria have been eliminated as endemic diseases from the North American continent. The last proved case of smallpox and the last clearly described outbreak occurred in Hidalgo County, Texas, in 1949.

Malaria, until the beginning of World War II a deeply entrenched endemic disease in the southern United States from Virginia to Texas, has been routed from these regions. The disease occurs sporadically anywhere in the country, usually among persons recently returned from malarious areas overseas. Only an occasional case appears in a person who has not traveled out of the country, and no residual focus of endemic infection exists.

Thus, while complete eradication perhaps has not yet been achieved and while introductions of malaria will continue to occur for many years, the position of those who argue that eradication cannot be achieved becomes purely semantic.

These same broad principles and issues apply to the field of veterinary medicine as generally as they do to human medicine. While this speaker has no personal experience or particular competence in veterinary problems, it is apparent that this field has led in the concepts of eradication.

Rinderpest, hoof and mouth disease, and glanders are brilliant examples of successful eradication. Bovine tuberculosis and brucellosis represent major programs with substantial success, even though complete eradication has yet to be achieved.

The continued application of the principles of epidemiology, intensive study of the factors determining the biological balance and the mechanisms for survival should make it possible for an organized program properly directed to achieve complete success.

In conducting an investigation of a local outbreak of disease, the epidemiologist should follow an orderly plan. His objective is to determine the reservoir or source of infection and the mode of spread in order to institute appropriate control methods. His problem is essentially similar to that of the clinician with a sick patient. He too must follow an orderly plan of taking a history, making a physical examination, instituting special laboratory procedures in order to reach a diagnosis. Only then can he institute proper treatment.

The following procedure is recommended to the epidemiologist:

1. Establish the existence of an epidemic. From the current count of reported cases, estimate gross attack rates and compare these with the normal rates for the same population during a similar period of time. Estimate the extent to which the current "epidemic" level exceeds expectancy. Sometimes false alarms occur or local factors have led to gross exaggeration of the problem.

2. Verify the diagnosis. Be sure the reported cases are real and not due to misdiagnosis. A clinical examination of a sample of cases, review of hospital or physicians' records may suffice. Laboratory reports may already be in existence. If not, prompt institution of laboratory confirmation is essential.

3. Collect Case Reports. Immediately institute the collection of individual case reports on all instances of the illness in the area. Minimum data should include: Name, age, sex, race, address, date of onset, attending physician, hospital admission, and such data as may be available for confirmation of diagnosis. Insure prompt reporting of all new cases as they may occur.

   These case reports may be submitted by practicing physicians if disease is notifiable, or may be requested on an emergency basis. Review of hospital admissions, telephone surveys of physicians or other data such as absenteeism from schools or industry, or sales of medicine at drug stores may be helpful sources of information on incidence.

4. Preliminary Epidemiological Review. Tabulate the case reports and orient their occurence in terms of time, place, and persons.

a. Time - Determine epidemic curve

b. Place - Determine epidemic area, seek limits to geographic localization. Prepare spot map and calculate attack rates by wards, census tracts or proper subdivisions in the area.

c. Persons - Determine incidence by age, sex, race, family units and such other population characteristics as may be available at the time.

5. Formulate Hypothesis. From the preliminary epidemiological review, a number of leads to the source and mode of spread should be apparent. Does the rough pattern correspond to a common vehicle outbreak, to an arthropod vector, or to contact? Formulate one or more hypotheses that are consistent with the data. Exclude those that are not consistent.

6. Test Hypothesis. Institute appropriate field studies to test this hypothesis or hypotheses. Usually this involves an individual case investigation of all or a random sample of the cases and often of suitable controls. Special studies of the environment will probably be necessary, such as an investigation of water, milk and food supplies, immunization status, social customs, special gatherings and occupational exposures. These special studies should only be undertaken as a result of leads provided by the preliminary epidemiological review, or as they arise from the ensuing detailed case studies.

   These special studies usually provide the confirmatory and clinching evidence you are seeking.

7. Establish Cause. Continue intensive investigation until evidence establishes soundness of one hypothesis and all other possible explanations can be excluded as inconsistent with the whole evidence.

8. Prepare a report. Summarize your investigation in an orderly report written so that intelligent laymen can understand it. Unless you can communicate your findings and conclusions to others in a convincing fashion, they are useless. Your report may well follow the outline recommended above for your investigation.

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EPIDEMIOLOGICAL ASPECTS OF TUBERCULOSIS CONTROL

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The incidence of bovine-type tuberculosis in man has declined to an all-time low in recent years. The last reported confirmed case occurred in 1957 in a rendering-slaughterhouse worker in western Massachusetts. The most recent proved case of disease in children was in 1954 in an Ohio farm boy, whose cervical adenitis was identified as tuberculosis on histopathological examination. (Table I)

Of the cases which have come to the attention of the Communicable Disease Center, it is noteworthy that most of the children had cervical adenitis or scrofula while the adults had pulmonary disease. The rarity of bovine-type tuberculosis as a clinical entity in man is most impressive in light of the hundreds of thousands of new tuberculosis infections and diseases which occur in man annually.

In some parts of Europe bovine tuberculosis continues to be an important cause of human disease. In south Wurtemberg (Germany), a heavily infected area, bovine tubercle bacilli were isolated from 19.2 percent of human patients with pulmonary tuberculosis and from 58.6 percent of patients with extra-pulmonary tuberculosis.

The incidence of pulmonary bovine-type tuberculosis was 9 percent in patients under 30 years of age, but 34 percent in those over 30. These 34 percent were nearly all workers in cattle byres.

Historically, tuberculosis in man and animals was first recognized as a serious public health problem almost 100 years ago. The first organized effort to control tuberculosis in animals and man was by veterinarians employed by municipal governments to clean up local milk supplies and remove diseased milch cows.

Milk sanitation and bovine tuberculosis control were the beginnings of many local health programs. Subsequently, these local bovine tuberculosis control programs developed into State-wide programs and these laid the foundations of a national program which was inaugurated in 1917 by the United States Bureau of Animal Industry.

A decline in the bovine-type infections in children was an early result of tuberculosis control of dairy cattle and the practice of milk pasteurization. The results in terms of improvement in child health were a potent force in persuading large cities to require official tuberculosis testing of all dairy cattle producing milk for human consumption.

Minneapolis was the first large city to require all milk entering the city to be from accredited herds. Soon afterward a number of other cities

adopted regulations which required all milk sold in their respective health jurisdictions to come from tuberculosis-free herds. The enactment of tuberculosis accreditation regulations by Chicago in 1926, followed quickly by other large cities, was the turning point which insured the success of the national campaign. By 1940 the entire country became a modified accredited area and the human form of bovine tuberculosis was disappearing.

With the decline in the incidence of bovine tuberculosis, the number of no-visible lesions reactors in cattle has steadily risen until they now account for about 75 percent of the total number of reactors. This situation is found not only in the United States but also occurs in all countries that are carrying on tuberculosis control campaigns. In Norway and Sweden this has become a major problem in tuberculosis eradication. Australia reports a similar situation.

The many causes of non-specific sensitization are well summarized by Francis and the audience is undoubtedly familiar with them. They include early infection followed by early recovery and sensitization to antigentically related organisms such as Mycobacterium tuberculosis avium, hominis, paratuberculosis, johnei, phlei, and recently, other acid-fast organisms, some of which are still unidentified.

Some of the more recently isolated groups may include such mycobacterium as the 607 strain, a saprophyte, and the Battey strain, a chromogenic acid-fast organism which causes sensitization and occasionally disease in man.

Epidemiological and epizootiological investigations are needed to determine the significance of these organisms that have come on the scene lately. In the human field, considerable research is being done by Edwards and Palmer of the Public Health Service on the distribution of non-specific tuberculin reactions in man. P.P.D. antigens are being made from some of these recently discovered acid-fast organisms for human testing. A similar study with NGL herds may be indicated.

The unravelling of the epidemiology of tuberculosis in man and animals is a major medical problem to both public health and livestock disease control authorities. Close cooperation and coordination in the study of these problems will accelerate the efforts of medical and veterinary epidemiologists.

At the national level, all parties concerned are desirous of finding the solution to the epidemiology of non-specific tuberculin reactors in man and animals.

Liaison between agriculture and health agencies should be encouraged among those who are studying similar situations. An example of this cooperation is the excellent support given by the Agricultural Research

Service tuberculosis control authorities to the studies on the serological status of tuberculin-positive cattle at the University of Iowa's Institute of Agricultural Medicine. These studies will attempt to evaluate the Parlett method for detection of tuberculosis antibodies in serum of tuberculin-positive cattle at the time of slaughter.

The Institute is also carrying on a recriprocal tuberculosis case finding project by visits to Iowa farms where reactor animals are identified. A number of States have inaugurated similar projects in recent years. An epidemiological investigation by local health authorities should be made any time animal tuberculosis is identified to determine possible evidence of tuberculosis in people who have had contact with the infected animals.

Bovine tuberculosis is communicable to man by both airborne and ingestion means, and may cause pulmonary as well as extra-pulmonary disease. When bovine-type phthisis occurs in man it can be transmitted to animals and man. Human-type disease occasionally is the cause of sensitization of cattle to tuberculin. As you know, the human-type organism seldom causes disease in cattle but produces an infection which results in a reaction to the tuberculin test.

The exchange of information on the prevalence of animal and human tuberculosis by State and local public health and livestock disease control officials will expedite the necessary investigations which are needed to eradicate this age-old scourge of man and animals.

It is also important that this information be disseminated among physicians and veterinarians so they will be aware of the problem at hand and can advise their patients and clients accordingly.

Table 1.--Reported Bovine Tuberculosis in Man 1948 - 1958

Year	Locality	Epidemiological Data	Human Illness	Remarks
1. 1948	Chicago, Ill.	Housewife. No known exposure. Raised in Iowa	Spinal tuberculosis beginning about 1941, which spread to the right shoulder and urinary tract.	Culture confirmed.
2. 1948	Northern Ohio	Child exposed to a diseased herd. 36 tuberculous cattle were removed. Most of these had gross lesions at slaughter.	Farm child had cervical adenitis as did a number of children in nearby town who used raw milk from the infected herd.	No organism recovered. Histopathological report revealed epitheloid tubercles.
3. 1948	New York	Farmer. Pulmonary tuberculosis identified in dairy herd.	Bovine type pulmonary tuberculosis.	Culture confirmed.
4. 1950	Southeast Kansas	Diseased dairy herd which was supplying raw milk to the community.	Sharp increase in positive tuberculin reactors among children who drank raw milk.	No clinical disease reported.
5. 1950	New London, Conn.	Housewife and secretary. No known exposure.	Bovine type pulmonary tuberculosis.	Culture confirmed.
6. 1951	Maine	Raised on a Canadian farm.	Aged individual suffering from cancer who also had pulmonary tuberculosis.	Culture confirmed.
7. 1951	Kanawha County West Virginia	Confined to a German labor camp, 1942-45, where she drank raw milk. Came to the U. S. as a war bride in 1948.	Bovine type pulmonary tuberculosis. First became ill in 1950.	Culture confirmed.

DHEW, PHS, BSS, CDC, VEterinary Section - Jan. 1959

Table 1.--Reported Bovine Tuberculosis in Man 1948 - 1958 (Continued)

Year	Locality	Epidemiological Data	Human Illness	Remarks
8. 1952	Kanawha County West Virginia	Son of above case	Two year old child developed tuberculosis meningitis.	No isolation reported.
9. 1953	Weirton, West Va.	Raw milk used.	Bovine type pulmonary tuberculosis in a 67 year old diabetic woman. Three years previously she had had a chest X-ray which was negative. Fatal case.	Culture confirmed.
10. 1954	Fayette, Ohio	Infected dairy herd on farm where he lived.	Six year old boy with cervical adenitis	Organism not isolated but histopathology revealed. caseating epithaloid tubercules.
11. 1955	Kentucky	Used raw milk	Six year old girl with cervical adenitis	Tuberculosis organism isolated but not typed.
12. 1957	Springfield, Mass.	Worker in an abattoir rendering plant.	Cervical adenitis	Culture confirmed.

PUBLIC STOCKYARDS INSPECTION

F. C. Mau, Animal Disease Eradication Division, ARS
Union Stockyards, Chicago, Illinois

At the present time there are 59 public stockyards located in 33 States operating under the inspection of the Animal Disease Eradication Division. I have had the opportunity of visiting many of these plants and of helping to establish uniform procedure in the inspectional operations and correlation of the Division's activities.

Among the many problems that arose at these stations were the methods and procedures to be followed in the handling of reactor cattle, and the tracing back to the farms those non-reactor cattle and swine that showed evidence of tuberculosis on post mortem examination.

In order to become a competent supervisor at any of these markets the veterinarian assigned to that particular market must be familiar with the trade territory which supports the market, the distribution of livestock, and be familiar with the trade practices of those engaged in the industry, including stockyard management, commission agencies, order buyers, and transportation companies.

For example, in stockyard management, the veterinarian should be familiar with methods and procedures for receiving, handling and weighing livestock and maintaining records.

In receiving, the operator should be encouraged to indicate on the receiving records whether consignment contains reactors and to see that the truck license is indicated on the consignment ticket. They do show the car number if the shipment originates with a railroad.

He should make sure that designated pens are provided for yarding reactor animals and that they are marked in such manner as to be known by those engaged in the industry. At the time of weighing the reactor tag numbers should be recorded on the weight ticket, and adequate records should be kept as to trucks that are cleaned, washed, and disinfected.

It is a responsibility of commission agencies to their customers to identify and maintain a good system of identification. Where reactors are involved, they are required to read the reactor tag number; and they will receive assistance from the inspectors in doing this part of the work. These numbers are to be checked against the accompanying quarantine form which is brought with the animals to market. In the event there is a discrepancy, or the reactor tag is missing, the right ear tag is to be used as a recording number.

In the case of non-reactors, at most stockyards the commission agencies follow a procedure of indicating the description of each animal

weighed. This is particularly true in the case of cows or bulls. The promptness with which these firms handle the salvage reports on indemnity-due reactors aids in the completion of indemnity papers and the receipt of money by the owner. As a whole, order-buying agencies understand what is required of them in moving livestock interstate. However, they are very dependent on the inspector to provide information regarding requirements to make such movement and in presenting their animals for inspection before certification.

When we come to the problem of transportation companies, railroads do not generally present difficulties in having their equipment presented for cleaning and disinfection when so required by the regulations.

Sometimes we are not so fortunate with the truck operators, although we have come a long way in educating this group to the necessity of compliance with the law. Most of the big line companies cooperate very well. It is the smaller concerns and the small private operator who must still be educated.

With this phase pretty well covered, I would like to offer a few suggestions. For example, in relation to accompanying papers, whether they are State forms or the ADE 1-27 form, I would suggest that the right ear tag as well as left ear tag be indicated on the form.

I would also like to suggest that these papers be delivered to the agency that is to handle the animals at the market, or if they are going direct to slaughter that they be presented to a responsible party at the slaughtering establishment.

It would be very helpful if a copy of the form were mailed to the man in charge of either the Meat Inspection Division operations or the Animal Disease Eradication Division, where the animal is consigned.

With reference to the cases reported on Animal Disease Eradication form 6-35, it is suggested that wherever it is practicable, and the animals involved have been purchased through one of the public stockyards under ADE Division inspection, that the report be sent to the ADE Division inspector for checking to determine the owner's name and address.

We are in a better position to get this information than most folks. The commission agencies feel freer to expose their records to us, although they are somewhat apprehensive about showing them to a packer. We also can check the weight ticket describing an animal. After we have procured the desired list of owners, together with the ADE form 6-35, it can be returned to the Meat Inspection Division for distribution to the proper authorities.

It is suggested that these forms be sent to the stockyard immediately following slaughter of the animal rather than to wait for laboratory

findings on specimens submitted on such cases. The reason for this is that while these incidents are fresh in the minds of everyone involved the animal can be more readily identified.

In passing, I would like to offer this suggestion to those engaged in Meat Inspection. Where the carcass is condemned and the weight is determined by estimating, it might be well to so indicate it on the report. Where the description of the animal is made available by retention of the hide, marks of identity such as paint marks, clip brands, or hot iron brands should be shown.

In the case of hot iron brands, you can call upon the stockyard inspector to help identify the brand if an animal was purchased at the stockyards located in the same city as the slaughtering plant, or if the packer purchased the animals direct. In some instances there is an accompanying brand certificate.

Where lesions are found in fat steers or heifers by those engaged in field activities, they should keep in mind in checking them out that the owner has a bill of sale from the original owner. These bills always show the brand, if any, number of head, the weight, and the price paid for the animal.

If the field veterinarian making the investigation will gather this information he can always check back through the selling agency, and if the animals were purchased at a public stockyard the ADE Division inspector can assist in tracing the animal back to the point of origin.

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FEDERAL MEAT INSPECTION AS AN AID TO TUBERCULOSIS ERADICATION

R. K. Somers, Meat Inspection Division
ARS, USDA, Washington, D. C.

Veterinarians conducting Federal meat inspection have had long experience in aiding the tuberculosis eradication program. It seemed natural for a veterinarian when he encountered an extensive case of tuberculosis to attempt to trace the origin of the animal and supply such information to someone who could use it. Occasionally this information was given to a health department but more frequently it was furnished to veterinarians who had the responsibility for disease eradication programs.

For a long time instructions concerning the handling of such cases were vague and non-existant at many locations and the meat inspection veterinarian could find nothing in his regulations which required him to do anything more than condemn the diseased carcass and supervise its destruction for human food.

The Federal Meat Inspection Regulations promulated under the Meat Inspection Act are for the purpose of assuring a wholesome food supply and do not contain authority for the meat inspection veterinarian to function as a part of some animal disease control or eradication program.

Arrangements were made under the Bureau of Animal Industry, and further elaborated under the Agricultural Research Service, for meat inspection veterinarians to perform certain services which could aid in the disease control program. The identification and tracing to point of origin of carcasses found to contain tuberculosis has become a very important part of this program. We believe that even more extensive use of this means of locating possible foci of infection can be developed.

One factor which would improve the effectiveness of this procedure would be the development of a more positive means of identifying cattle which are sent to slaughter.

It would be a simple matter if each animal coming to market carried a shipping tag with the name and address of the sender. However, it must be remembered that dairy cattle are generally not sent to slaughter unless the animal has lost its usefulness for the purpose intended. Sending such animals to slaughter is a normal way of disposing of them and the condition which terminated the animal's usefulness may very well be one that is not very readily

apparent so the seller would expect to collect at the regular market price for the animal.

There is always a possibility that the purchaser might try to avoid payment if the animal was condemned provided the name of the owner could not be identified with certainty. Also it appears natural for any seller to attempt to avoid identification of merchandise that is not of good quality.

Ear tags used in identifying animals which are tested or vaccinated have served to be a good means of identifying dairy animals and should continue to make this procedure practical. However, a means of improving its effectiveness would be for the area supervisor to get acquainted with meat inspection veterinarians and encourage cooperation through friendly discussions.

In the meantime we in the Meat Inspection Division are endeavoring to improve the diagnostic ability of our veterinarians. However, this may be difficult if the tuberculosis eradication program achieves its goal and there are no lesions available for training material.

Veterinarians in meat inspection have also been assisting the disease control program by furnishing supervision over the cleaning and disinfection of vehicles used to haul reactor animals. From experience we have seen that many truckers will maintain their equipment in a clean and sanitary condition but we have also noted that some supervision over cleaning is required to get a completely satisfactory job done.

The disposal of condemned material in Federally inspected plants is handled in such a manner that diseased material, such as tuberculous lesions, is destroyed by rendering at high temperatures which kills the organisms.

You should be aware, however, of the growing demand for inedible and condemned material for use in the raw state as animal food. Up to this time, material used for this purpose has not been apparently affected with an infectious disease or septic condition. However, we would have no justification under the Meat Inspection Act for denying permission to use such material if it was destroyed for human food by denaturing with dye or finely powdered charcoal and if facilities were provided for handling it in a manner which would preclude contamination of edible products.

LABORATORY SERVICES AS AN AID TO TUBERCULOSIS ERADICATION

Wayne D. Yoder, ADE Div. Diagnostic Laboratory
ARS, USDA, Ames, Iowa

All veterinarians, those in practice as well as those veterinarians involved in disease eradication, have become increasingly aware of the value of accurate diagnosis in their work. This has increased their reliance on laboratories for help in confirming the diagnosis which they have made.

With the decrease in the amount of tuberculosis in our herds, there has been an increase in the number of disturbing factors arising which will, at times, cause us to question some of the tests which we have previously relied upon.

In such cases the laboratory can assist in confirming a diagnosis. This will be our main function in the Animal Disease Eradication Diagnostic Laboratory at Ames, Iowa. We will have other problems involving other diseases, but I am confining my remarks to tuberculosis.

In those instances where it is desirable to know the type of tuberculosis involved, we are in a position to carry this out. As you know, typing depends primarily upon the inoculation of suitable laboratory animals. Thus, the typing of the organism will take at least 4 weeks and in some instances it will be 8 weeks before the answer is known.

In connection with the typing, it might be mentioned that research being carried on in several research centers indicates that there are several other tests which may prove to be reliable in typing.

Histopathological studies of infected tissues are valuable in making a post mortem diagnosis of tuberculosis. The typical granulomatous reaction revealed in properly stained tissues helps in making a definite diagnosis. Also, histopathological work enables one to diagnose other conditions which may be confused with tuberculosis. We have a pathologist at the Animal Disease Eradication Division Diagnostic Laboratory who is well acquainted with histopathological techniques used in disease diagnosis.

Another aid which will be available is the possible culture of the tuberculosis organisms from tissues submitted. Culturing of tissues may lead to evidence indicating the presence of other acid-fast organisms which may complicate tuberculosis testing.

Along this line, certain serological tests now being reported in the literature may aid in tuberculosis diagnosis and typing. Two of the possibilities in this respect are the hemagglutination test and the agar double diffusion precipitation test.

Another factor which at times can be confusing is the presence of systemic fungus diseases. The systemic fungus diseases at times may cause lesions which grossly may resemble tuberculosis. The two main fungus infections involved are lesions caused by Histoplasma capsulatum and Coccidioides immitis.

The Diagnostic Laboratory at Ames is now training its personnel in the necessary techniques in diagnosing fungus infections. Here again, histopathological techniques as well as cultural studies will be important in diagnosing the infection present.

The exact importance of the fungus infections across the country is not known, but it is a condition which should not be overlooked. Although tuberculosis has been recognized as a public health problem for years, the systemic fungus infections are now being given necessary study as a public health problem.

In summary it can be said that our laboratory is now ready to assist in the pressing tuberculosis problems present in the various States. However, we will be depending as always upon the man in the field to carefully select his cases and present them to the laboratory with as complete a history as possible. Also, it should not be construed from the foregoing that every herd tested for tuberculosis and found infected should have laboratory studies made.

INTERSTATE REGULATIONS

J. J. Martin, Animal Disease Eradication Division
ARS, USDA, Washington, D. C.

The authority for the regulations of the Department of Agriculture governing the interstate movement of livestock is contained in the so-called Animal Quarantine Laws of 1884, 1903, and 1905. In later years additional authority was granted by Congress as the need arose.

Obviously the Federal regulations cannot be any broader than the authority on which they are based. A violation of the Animal Quarantine Laws is a criminal offense. However, it is necessary for the Government to prove beyond a reasonable doubt that the crime was committed.

Prior to the establishment of the Bureau of Animal Industry in 1884, the problem of eradicating infectious livestock diseases was one for the State or States involved to cope with individually. At that time it was a difficult task for a State that apparently had eradicated an infectious disease to keep from becoming reinfected by animals from neighboring States.

In addition, there was always the question as to whether a specific infectious disease actually existed in a given State because livestock officials were hesitant to acknowledge the existence of an infectious disease for fear of an embargo or other reprisal. Also, some States were not in a position, from a financial standpoint, to stand the expense of eradicating an infectious disease that had become widespread.

It was largely these circumstances, as well as embargoes against American livestock by foreign countries, that brought about the establishment of the Bureau of Animal Industry by the Act of May 29, 1884.

Among other things, this Act provided for the Commissioner of Agriculture:

1. To make regulations necessary for the suppression and extirpation of contagious, infectious, and communicable disease of livestock.

2. To expend Federal funds for investigation, disinfection, and quarantine measures in cooperation with States in the extirpation of infectious diseases. This was later extended to include expenditures of Federal funds for eradication and payment of indemnities when a cooperative agreement was entered into between the Department of Agriculture and a properly constituted State authority.

3. To make investigations as to the existence of such livestock diseases.

4. To notify in writing transportation companies and publish in newspapers notice of the existence of contagious, infectious, or communicable diseases.

The Act prohibits the interstate movement of animals known to be affected with a contagious, infectious, or communicable disease, when it states "that no railroad company . . . shall receive for transportation or transport . . . nor shall any person . . . deliver for such transportation . . . nor shall any person drive on foot or transport in private conveyance any livestock, knowing them to be affected with any contagious, infectious, or communicable disease."

It was under this authority that the bovine tuberculosis eradication program in the United States began in May, 1917. On November 1, 1940, a little more than 23 years later, all counties in the United States and the Territories of Puerto Rico and the Virgin Islands were rated as modified accredited areas, signifying that bovine tuberculosis among cattle in such areas had been reduced to less than 0.5 percent. To accomplish this it required the slaughter of almost four million reactors.

Because of the prohibition against the interstate movement of diseased livestock, it was necessary in 1920 to request Congress for specific authority to permit the interstate movement of cattle reacting to the tuberculin test. At that time the large number of reactors made it difficult to dispose of them within the State where found. In addition, the salvage price was being continually lowered.

Under this new authority the Secretary of Agriculture prescribed rules and regulations for the interstate movement of reactors, which required that the animals be tagged, branded, accompanied by a certificate, and shipped to public stockyards or slaughtering establishments operating under Federal inspection. Violations of these regulations have included failure to comply with one or a combination of the above requirements.

There were no Federal quarantined areas established in the tuberculosis eradication program. Complete reliance was placed on State quarantines. As the program progressed, the need for handling cattle from accredited areas separate and apart from those from non-accredited areas became apparent. This was particularly true at public stockyards where it was required that separate pens be set aside for the receipt of cattle from non-modified accredited areas.

Since November, 1940, when the whole country reached an accredited status, there has been practically no Federal requirement for the interstate movement of cattle under the tuberculosis regulations with the exception, of course, of reactors.

Because of the problems that have arisen during the past few years, the following changes in the Federal regulations are under consideration:

1. Definite requirements for the reaccreditation of areas, and to provide for the removal from the accreditation list of any area that is overdue and in which no steps are being taken to retest the required number of cattle necessary to ascertain if the area qualifies for reaccreditation.

2. Control over the interstate movement of cattle exposed to tuberculosis because of having been in a herd under State quarantine.

For some years after the whole country reached the accreditation status it was more or less taken for granted that bovine tuberculosis would soon be completely eradicated. However, as you know, this has failed to come about, and we still are finding many cases of tuberculosis in cattle.

It is hoped that the new Federal tuberculosis regulations soon to be published will strengthen the eradication program and help to bring about better control over the interstate movement of cattle insofar as tuberculosis is concerned.

SUMMARY EVALUATION OF CLINICAL RESULTS

E. A. Schilf, Animal Disease Eradication Division
ARS, USDA, Madison, Wis.

In the past several days, we've been here discussing and working with the various phases of tuberculosis eradication work. I like to think of this conference as a period in which we have examined the tool kit with which we will eradicate tuberculosis. In looking over this kit, it would appear that we have standardized the tools so that we can go back home dedicated to the thought that we can eradicate tuberculosis.

Now, we're not only going to have that thought, but we're going to have to pass it on to the various practitioners and other regulatory people with whom we are working.

If we have our tools perfectly standardized we will more nearly obtain standard work. Therefore, the man in the Atlantic coast area who does TB work will operate identically with the man in California who is working on tuberculosis eradication.

It is imperative that we carry this information on to the men in our areas. If it didn't go beyond this group, some good would be done But think how much good it can do if, when we return home, we pass the information on to all veterinarians in our area.

In tuberculosis testing, I like to think that there are three factors involved; the tuberculin, you, and the cow. The tuberculin is standardized regularly. Each lot of tuberculin, we are told, is put through its various tests to insure we have similar antigenicity The cow is a variable, and one that we can't do a whole lot about. You and I--in the middle--are perhaps the ones in the process that should not vary.

We have various prescribed sites for injecting tuberculin. The manual tells us that we use 0.1cc in area testing and 0.2cc in infected herd testing. We must stick to these accurate dosages. The guide for tuberculin testing further prescribes the reading of reactions which we should use as our standard.

Earlier in the week we got together and checked over our equipment. There is no question that most of us have a pet syringe that we like to use. We get the feel of it, and we stay with it. We have certainly checked the dosage delivery of that pet syringe because it is important that we know we are always giving the prescribed dose and that it is being injected in the right place.

What is the right place? Here is another thing that we have a tendency to get a little bit careless about. One of the things that will help us is restraining the cow. If we have our cow under good restraint, we're going to be able to make that injection where we want it and use the exact dose of tuberculin that we want to give. In the case of the caudal fold, we definitely want it in an area where we're out of the hairline, in a hair-free area. In the case of vulva injection, we want that injection made at the junction of the mucus membrane with the external epithelium.

We were looking at some of the other equipment that we had in the kit. One of the problems was needles. We had quite an array of needles there. The men who use the coarser short needle have indicated that they were unable to get any other needles. It had been issued to them by their office. However, it is my understanding that through the work of our Washington tuberculosis eradication section the prescribed needle is now on the market.

In Wisconsin we have purchased some of the prescribed three-eighths-inch 26-gauge needles. In the future, if those of you who are tuberculosis testing will request that standard needle and you should receive it. If you take it up with your veterinarian-in-charge, I am certain that he will arrange for you to get the right needle.

On that first afternoon, before we started with the actual tuberculin injection, we had an opportunity to make as many injections as we wanted in our two practice cows, using saline solution. We had an opportunity to make caudal injections and many, many cervical injections. When we were satisfied that we were making cervical injections without bending too many needles we started our demonstration cows using tuberculin.

These cows had been previously sensitized with a suspension of killed M. tuberculosis. The test cattle were injected intradermally in the caudal fold and vulva, on the right sides with 0.1cc of tuberculin, and the left sides with 0.2cc of saline.

At the site of the tuberculin injection reactions of various sizes were obtained at 72 hours, but when pure saline was injected there was no evidence of an injection having been made.

The demonstration cow was injected cervically. We have diagrams of the cow showing our cervical injection sites and comparative reaction sizes. At the first location, 0.05cc of tuberculin was injected, and the reaction was about 3/4-inch in diameter and was raised about 1/4-inch. At the second location we injected 0.1cc of tuberculin. This reaction was approximately 1-1/2 inches in diameter, and raised slightly over 1/4-inch.

At the third site, 0.2cc of tuberculin was injected. As expected, the reaction was greater than the other two. This reaction was 2 inches in diameter and raised ½-inch. At the fourth location, 0.4cc of tuberculin was used and a massive reaction was obtained. In our own cow, this reaction was 3½ inches in diameter and raised about 1 inch. This reaction irritated the cow considerably, and she became very sensitive to any palpation of the reaction.

At the site of the fifth injection we went back to our standard 0.2cc of tuberculin, but we added o.8cc of saline to make an injection total of 1cc to try to confuse the issue. We did not confuse the cow, and it was amazing how regularly these reactions resembled the 0.2cc injection of tuberculin.

At the sixth location on the left side we again injected 0.2cc of tuberculin to establish a standard. Reactions were about the same as on the other side in positions three and five where we also used 0.2cc of tuberculin. Positions seven, eight and nine were injected with increasingly diluted tuberculin. At the seventh position we used 0.2cc of 1-to-10 tuberculin saline solution, at position eight, Q.2cc of 1-to-50 tuberculin saline solution and at position nine, 0.2cc of 1-to-100 tuberculin saline solution. The reactions were progressively smaller, number seven being about 3/4-inch in diameter, number eight about ½-inch, and number nine about 3/16-inch, or a 1P reaction.

From the reaction obtained, it is readily apparent that the volume of the solution injected had no effect on the reaction. The reaction is dependent entirely upon the amount of tuberculin injected intradermally. Therefore, we had the same size reaction in locations three, five and six. As you see there is no more variation that you might expect free hand in drawing. To further point out the fact that the reaction is due to tuberculin, there was only one demonstration animal in which location number four was not the largest reaction that we had. And in every case, location number nine was the smallest reaction that we had.

Since these results so definitely indicate that the size of the reaction depends very definitely on the amount of tuberculin that is injected, it just stands to reason that we must routinely use a standard dosage of tuberculin when we are on area tuberculin testing or infected herd retesting. In all our testing, we must use a standard dosage to get comparable results. And, as I have said before, and as the manual indicates, it is 0.1cc of tuberculin for area testing and 0.2cc of tuberculin for infected herd retesting.

I mentioned earlier that when we came here one of the first things we did was to look over our tool kits. I think we did a little more than look it over. Lisening to these men, and feeling the various reactions in our clinical demonstration animals, I think perhaps we added a hone to our tool kit. Now we not only have the tools, but we have the equipment to sharpen them and keep them sharp.

When we go back home, let's look over these things from time to time, get out our notes, study them over, look at our diagrams and see if we can't spread the news that tuberculosis can be eradicated. Then go out and do the job.

SUMMARIZATION OF THE TUBERCULOSIS ERADICATION CONFERENCE AT LANSING, MICH.

C. D. Van Houweling, Office of the Administrator
ARS, USDA, Washington, D. C.

Since I was not able to be with you for part of the conference, it is somewhat against my better judgment that I have been persuaded to assume the responsibility of giving you my impressions and a summarization of the entire conference.

First of all, I think it would be fair to say that this may be the most important tuberculosis meeting that has been held in the United States since the country became completely modified accredited in 1940. My reason for saying this is that, as the program is now operating, we have come to the place where we will have to do something more than we have been doing if we are to go forward and succeed in eradicating bovine tuberculosis from the United States.

Recognizing this need, we realized that one of the first things we had to do was to change the complacent attitude in regard to this program. We made the first step in that direction last year. At the time of the United States Livestock Sanitary Association meeting in St. Louis we invited all the Federal Veterinarians in Charge in the United States and Puerto Rico to come to St. Louis a few days early. We spent the better part of two days discussing our tuberculosis and brucellosis programs. Our thought was that we should get the ideas and suggestions of the people who were in charge of the work at the State level on both of these programs.

That was the beginning of what we visualize as the "New Look," or a new approach to the tuberculosis eradication program. We recognized at that time that that was only the beginning, that we would have to go on from that point with other meetings and other work conferences to carry this story further.

Step number two is one of bringing together one man from our force in each of the States to give him the best information that we can provide by getting experts as speakers and instructors and using our own people on our research and regulatory staffs.

In this way we will have one man in each State who will have the advantage of the best information we have available on how the tuberculosis control and eradication program should be carried out in each State.

We know that this alone is not going to accomplish the job that we have in mind. We're going to have to have a meeting or meetings of State officials, at which time we will have the opportunity to lay before them the problem as we have seen it and discussed it this week. We wanted to

have someone from each of the State's forces at this meeting, but it became somewhat of a physical impossibility.

At one time we considered having a State and a Federal man here from only half the States, because we just didn't think we could handle 96 people in the clinical demonstrations of the program. However, we finally decided that we should limit it to the 48 that we have had here. But we know that we will have to have some other meetings to discuss future goals. Whether these meetings should best be conducted on a regional basis, State by State, or another national meeting, is one of the things we will have to discuss with the Tuberculosis Committee of the United States Livestock Sanitary Association and others who are vitally interested.

Now, some of you are beginning to think at this point that we are forgetting all about industry. After all, they are the most vitally concerned in the program. I'm the first one to agree that you have to have industry support. But it is our opinion that, until we have a program that is agreed upon, until we are ready to present the "New Look," we shouldn't go to the industry. This would be just presenting them with our problems, and they have plenty of problems of their own.

When we have a program that we think will do the job, then we ought to lay it out to them and invite their support and see whether they are willing to go along with us in regard to this disease. That is our long-range plan for carrying on this fight and eventually completely eliminating the disease.

Earlier in this meeting the objectives of the conference were outlined. I am probably repeating some of the same things that I have said already; that we wanted to assemble the best information and the best authorities we could to give you the latest and the best we have in regard to this whole program.

There are still some areas that have not been completely resolved. We've got some more work to do, but at least you've been exposed to the best that we can bring to your attention.

If you recall, about the first thing you were told was that we still haven't eradicated tuberculosis from the cattle of the United States. We first became complacent about our accomplishments back in 1940. This morning I was handed an article from the Milk Plant Monthly of December, 1940. The headline on this article reads: "No More Bovine Tuberculosis."

It says that, with the completion of the area testing program in the last two counties, King and Merced, in the last State, California, that all States and counties and the entire United States are now practically free from bovine tuberculosis. The degree of infection in every

county in every State has now been reduced to less than one-half of one percent, signifying practical eradication. And it goes on to say, and this is the exact quote: "From now on the testing will consist largely of precautionary retesting."

I don't suppose too many of you remember that release or remember that kind of thinking in 1940. And I don't think we should be too hard on the people who did think that way, because it's easy to adopt that frame of mind. It is possible to see, I think, why some people have been under the impression that the job was done, and we probably are going to have some difficulty in convincing the industry that we still have quite a long way to go.

At this conference you've heard a Director of Agriculture, a State Livestock Sanitary Official, and a Federal Veterinarian in Charge all tell you that the job was not done. There is still a job to do. You also had outlined for you some of the principles of sound disease eradication, and I'm sure that you were told that those general principles of disease eradication apply just as well to bovine tuberculosis as they do to any other disease.

You have heard quite a little discussion about our tuberculin, how we have striven to standardize the tuberculin we are now using, and how the men have worked over the years to make the tuberculin the best product that can be made. But I think we should recognize that, no matter how good the tuberculin is, no matter how standard it is, it's no better than the man who is using it. Regardless of how hard we work to improve the quality of tuberculin, it is still going to depend on the man who is using it.

You have also heard some discussion of the responsibility that our entire profession has in regard to this program. You heard a good discussion of how the colleges and schools of veterinary medicine contribute to all of the regulatory work, and particularly the tuberculosis program. You also heard a discussion of the practitioners' responsibility and I am sure that we must always give consideration to our own responsibility in regard to the service provided by practitioners.

From this point on, I'm going to be mainly talking to our veterinarians from the various States who have come to this conference. It is our responsibility to see that the State, Federal, and accredited veterinarians carry out the work according to approved procedures and in the manner in which we want them to carry it out.

You have been instructed in regard to the techniques of applying the tuberculin tests. You've had lectures, seen applications, and you've had an opportunity to apply the test yourself. You men are going to receive additional training at the hands of the best men we can find. And this is all to achieve, as nearly as we can, uniform procedures in the application and interpretation of the tuberculin tests.

We're very fortunate to have had a very complete review of the bacteriology of the tubercle bacillus, or bacilli, and some of the other acid-fast organisms that give us some trouble in our tuberculosis program and tests. Also, we have reviewed the mechanism of infection and resistance to pathogenic bacilli, and particularly the tubercle bacilli.

You've heard discussions and seen some demonstrations of cleaning and disinfecting procedures, heard discussion of what you might refer to as mechanical aspects of the program -- quarantines, handling of suspect herds, the cervical tests, the retest schedules, and how to maintain the integrity and the confidence of other people and ourselves in our accredited areas.

All those things have been discussed, and I hope that you have gotten a great deal from them. One of the most interesting sessions that I attended was the detailed study that was given to the pathological lesions resulting from the invasion of the tubercle bacilli. I doubt whether we could have had a better demonstration.

It was demonstrated to us how easily small lesions can be overlooked and how, with more careful and detailed examination, some lesions can be found in these cases that are generally referred to as NVL's, or more recently, NGL's. In this connection I think it's worth noting that this might partly explain the rather high percentage of NGL's.

Probably, if we had the time to search longer and harder in each of these cases, the ratio of NGL's to the number of reactors removed would not be as high.

We saw a properly conducted meat inspection examination as it is routinely conducted on these animals and those who presented the demonstration should be commended. Perhaps we could come up with quite a lot more lesions than we have been if we had the time for a more detailed post-mortem examination. And in addition, you were told how to collect your samples and how to submit them.

Also, you've been having a pretty thorough discussion of epidemiology and epizootiology. This is a very, very important part of the program as we get to the terminal stage. I think you now know what we mean by an epizootiological investigation in regard to TB reactors and TB suspects.

I was impressed this morning with the example that was given the thoroughness that's required if you're going to go the last mile in finding exposed animals in an exposed herd.

We think that the epizootiology of these infections and the investigations that must be carried out are extremely important, and I don't think we can overemphasize the importance of complete diligence and

perseverance in regard to those investigations. Now, today, you heard some more about the aids available to assist you in the eradication of tuberculosis.

I believe that more or less summarizes the conference up to the present point. To our men who have been assembled here and who are going on to training, I think I can tell you with all sincerity that, by the time you finish your training, we think you're going to be the best trained men in the United States as far as bovine tuberculosis is concerned. That is our objective.

You'll be recognized, as far as we are concerned, as the expert on TB in each State, having been exposed to the best information and training that we can give you.

Now, what are you going to do about it when you get home? I've had several people speak to me about this. We do not want you to go home with the idea that you are to change the program. First of all, the Animal Disease Eradication Division doesn't have the authority to change the program and it has no desire to make radical changes in the program. What we would like to have you do -- and we'll notify our Veterinarians in Charge in each State -- is to give you an opportunity to report to him and review the training you've received. If he wishes, he may invite other people in to hear your report. Then it will be up to him to plan your future activities.

Don't go back and immediately begin to instigate any program changes affecting policy. I think everyone will agree that we can do a better job than we have with the present program. That's not a change, it's just an improvement.

Don't give the impression that the program has been changed. The tuberculosis eradication program hasn't been changed. We are still operating under the same uniform methods and rules that we've been operaating under all the time. We've sent instructions out before in regard to the way the program should be carried on in regard to the tests, quarantining, and cleaning and disinfection. This should simply help to perfect those instructions.

I urge you again, don't go back and give the impression that the Animal Disease Eradication Division has taken over the tuberculosis eradication program. Nothing could be farther from the truth. We recognize that we are working in the States in cooperation with the States, under their laws and regulations. And we want the program that results in each State to be the development of the State and Federal veterinarian in Charge.

What is our attitude going to be as we go from this conference? First of all, I would like to make a comment that I've been on the verge

of making since I came here. Some of you probably feel that there's a big gap between the expressions given by some of the experts at this meeting and the policy that we've been advocating to you. That isn't true. We're the first ones to admit that we need additional information about tuberculosis in cattle and the other species as well. We need a better test if one can be developed. We need a better method of diagnosis and we need other information that we don't have.

We have asked a committee of the experts at this conference to give consideration as to what studies and what projects should be carried on to get the information we need. We realize there is a need for more information, but the point we're trying to get across is that we can do better than we have been doing with the tools that we have.

We think there is room for more carefully standardizing and unifying our testing procedures. And there is room for much better supervision of the work all up and down the line. Those are the things that we want you to stress.

We think, too, there is room for better cleaning and disinfection. Our cleaning and disinfection has to be done better than we've been doing it. This may be the source of some of the trouble we have in our so-called "problem herds."

We know that we need a better system for identification and tracing of animals, particularly those that are reported by meat inspectors as being lesion cases. I think we've stressed that enough already, but there are other techniques that can be used. Actually, it is probably perseverance and diligence that we need more than anything else in this regard.

One other thing I'm sure we want to give careful consideration to is the length of time that we maintain control over known infected herds. How long should they be under absolute quarantine before we turn them loose, and how long should it be before we can discontinue our checking on a six-month basis?

As I said before, you will be participating in some of the future meetings that we will hold. At this time I don't know whether we are going to hold regional or State meetings, but you men who have had this special training are going to be called on in your State to pass on the benefit of your training and experience to others.

I think that, as far as I'm concerned, this summarizes the conference, and concludes what I have to say to you.

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